STIC-Biotech/ChemLib 10/019,743

From: Carlson, Karen
Sent: Thursday, June 03, 2004 3:01 PM
To: STIC-Biotech/ChemLib
Subject: 10/019,743

Please search

the LH-RH derivative is a peptide represented by the formula

5-oxo-Pro-His-Trp-Ser-Tyr-Y-Leu-Arg-Pro-Z

wherein indicates residue selected from DLeu, DAla,DTrp, DSer(tBu), D2Nal and DHis(ImBz1), and Z indicates NH-C2H5 or Gly-NH2, respectively,

AND
the LH-RH formula derivative
5-oxo-Pro-His-Trp-Ser-Tyr-DLeu-Leu-Arg-Pro-NH-C2H5

Thank you!
Print out please.

Karen Cochrane Carlson
AU 1653
REM 3D85
Mailbox REM 3C70

Point of Contact:
Alexandra Waclawiw
Searcher: Technical Info. Specialist
Phone: CM1 6A02 Tel: 308-4491
Location:
Date Picked Up: 6-10-04
Date Completed: 6-16-04
Searcher Prep/Review: 2
Clerical:
Online time: 60

TYPE OF SEARCH:
NA Sequences:
AA Sequences:
Structures: 2
Bibliographic:
Litigation:
Full text:
Patent Family:
Other:

VENDOR/COST (where applic.)
STN:
DIALOG:
Questel/Orbit:
DRLink:
Lexis/Nexis:
Sequence Sys.:
WWW/Internet:
Other (specify):

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=> d his

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                ACT CARLSON/A
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L2            103 SEA FILE=REGISTRY CSS FUL L1
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                ACT CARLSON2/A
                ---------
L3               STR
L4   (       103)SEA FILE=REGISTRY CSS FUL L3
L5               STR
L6   (        25)SEA FILE=REGISTRY SUB=L4 SSS FUL L5
L7   (        22)SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND D
L8            22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND D(3S) (LEU OR LEUCINE)
L9             1 S 74381-53-6
L10            1 S 53714-56-0
L11           20 S L8 NOT (L9 OR L10)

     FILE 'CAPLUS' ENTERED AT 14:07:32 ON 10 JUN 2004
L12         3640 S L2
L13          226 S L9 NOT (1999-2004)/PY
L14          312 S L10 NOT (1999-2004)/PY
L15           13 S L11
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FILE 'REGISTRY' ENTERED AT 14:11:06 ON 10 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     9 JUN 2004  HIGHEST RN 691352-46-2
DICTIONARY FILE UPDATES:    9 JUN 2004  HIGHEST RN 691352-46-2

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d que stat l2                                  Sequence with 1 and 2.
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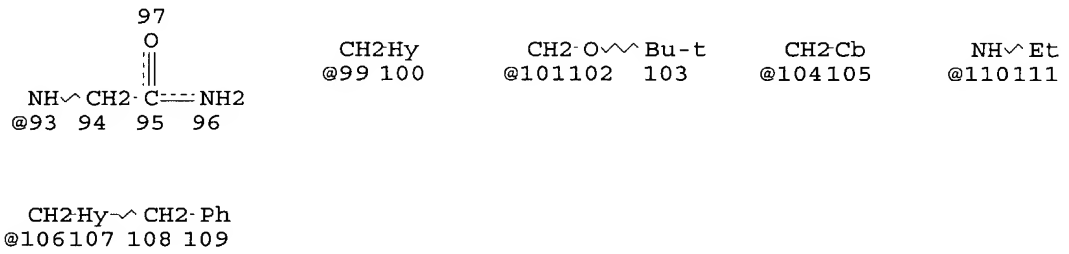

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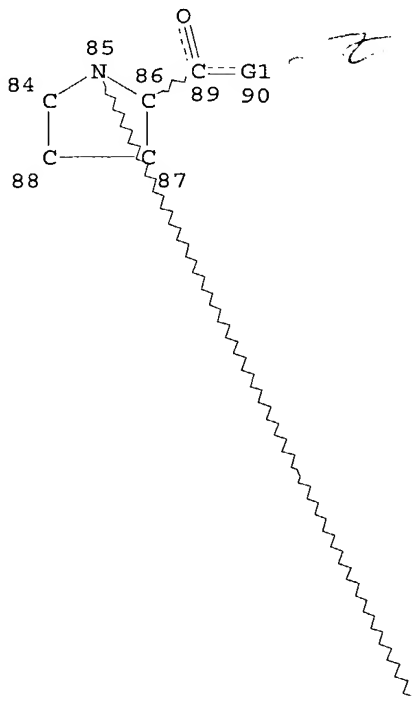
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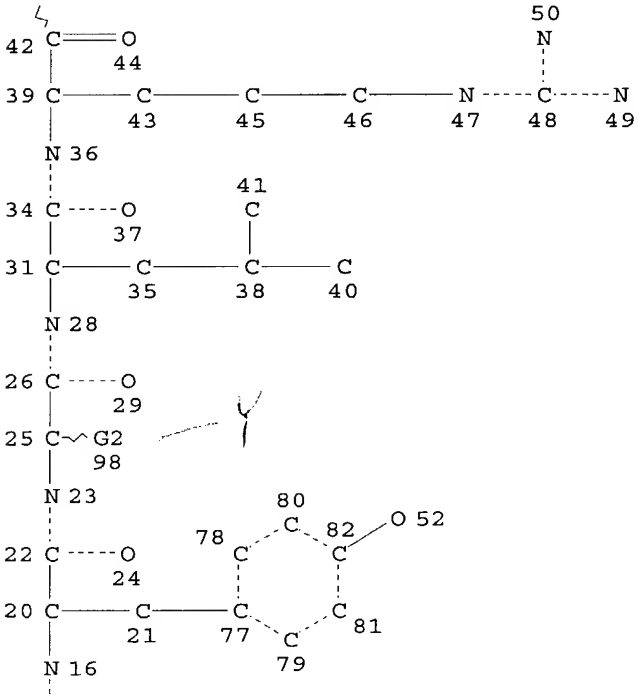
Page 2-A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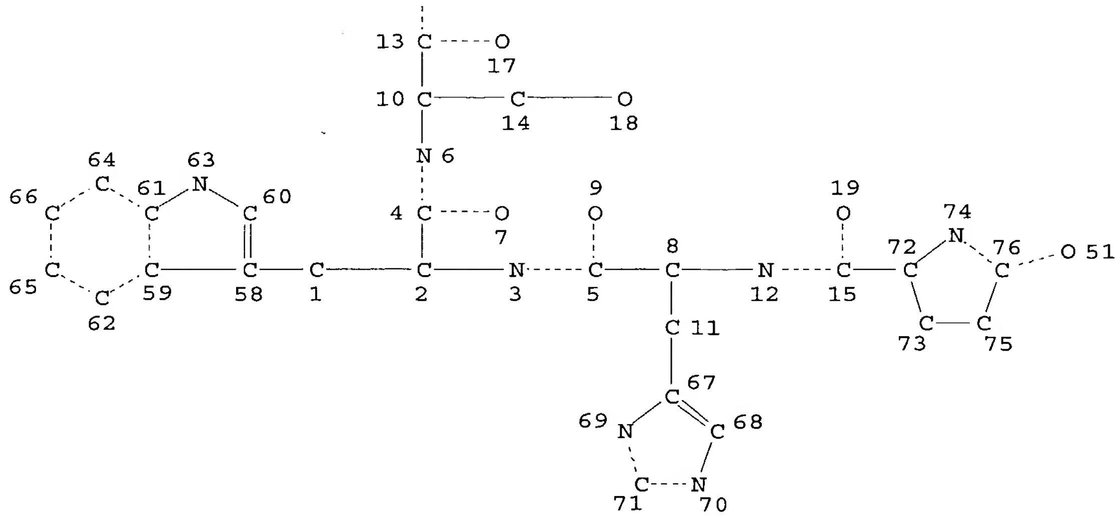

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GGCAT IS PCY UNS AT 105
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DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E8 C E1 N AT 100
ECOUNT IS E3 C E2 N AT 107

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 100

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 1298 ITERATIONS 103 ANSWERS
SEARCH TIME: 00.00.01

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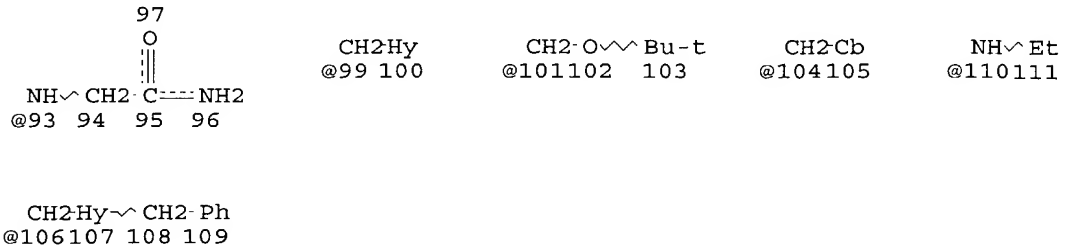
→ specific sequence where Y and Z are defined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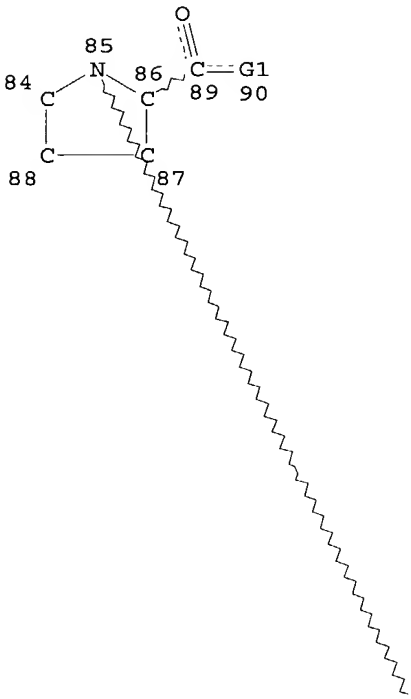
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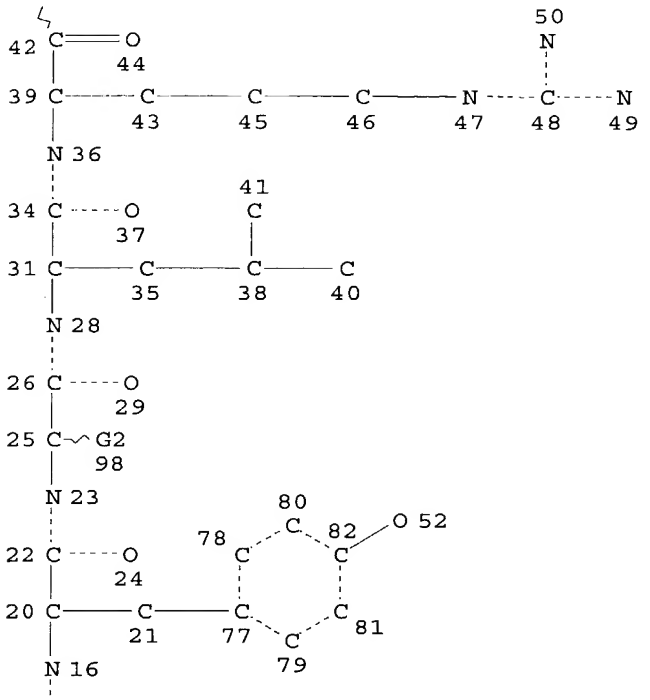
Page 2-A



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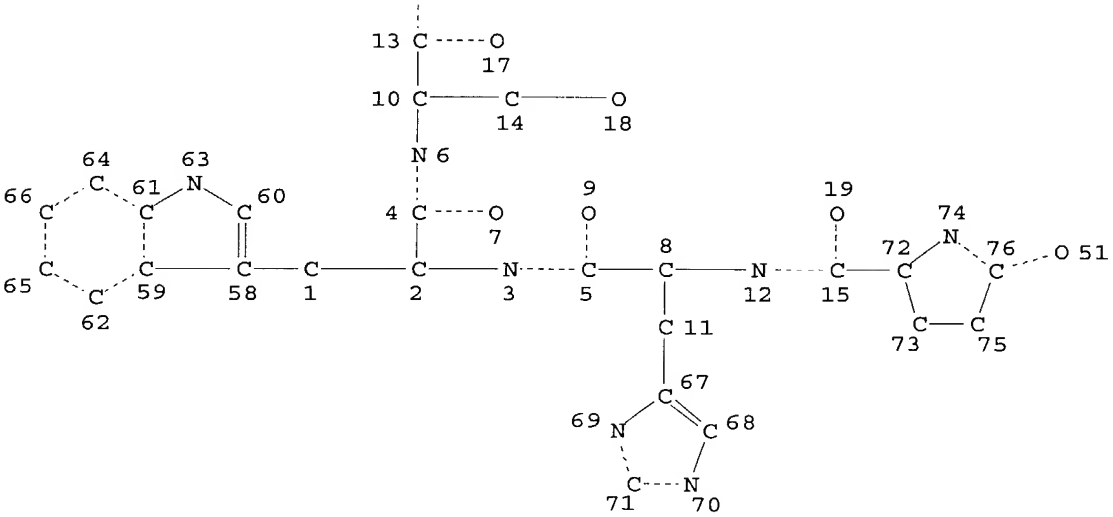

Page 4-A
VAR G1=110/93
VAR G2=I-BU/ME/99/101/104/106
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS PCY UNS AT 100
GGCAT IS PCY UNS AT 105

GGCAT IS MCY UNS AT 107
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E8 C E1 N AT 100
ECOUNT IS E3 C E2 N AT 107

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 100

STEREO ATTRIBUTES: NONE
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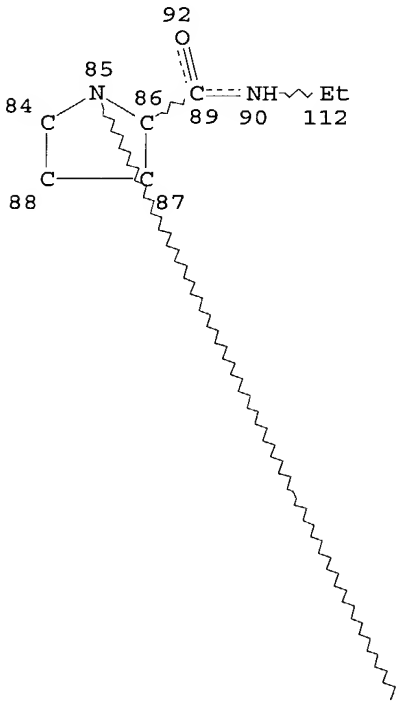
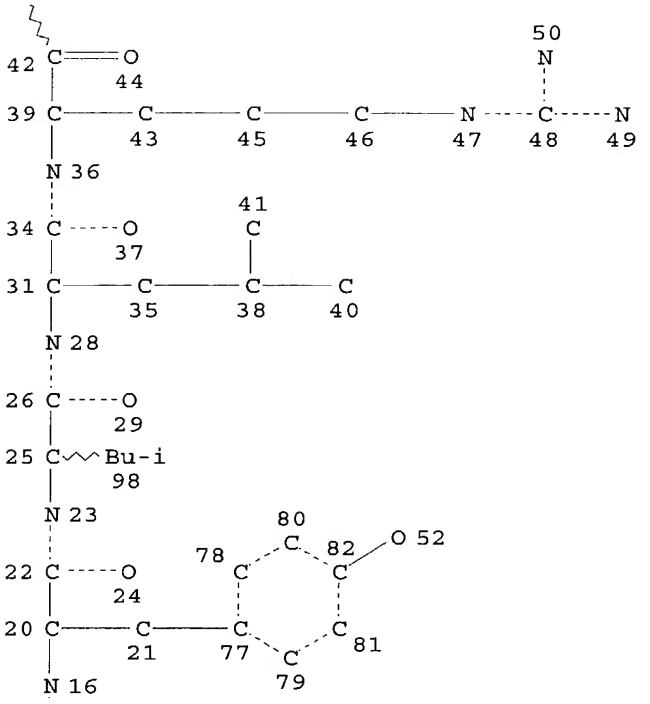
L5 STR





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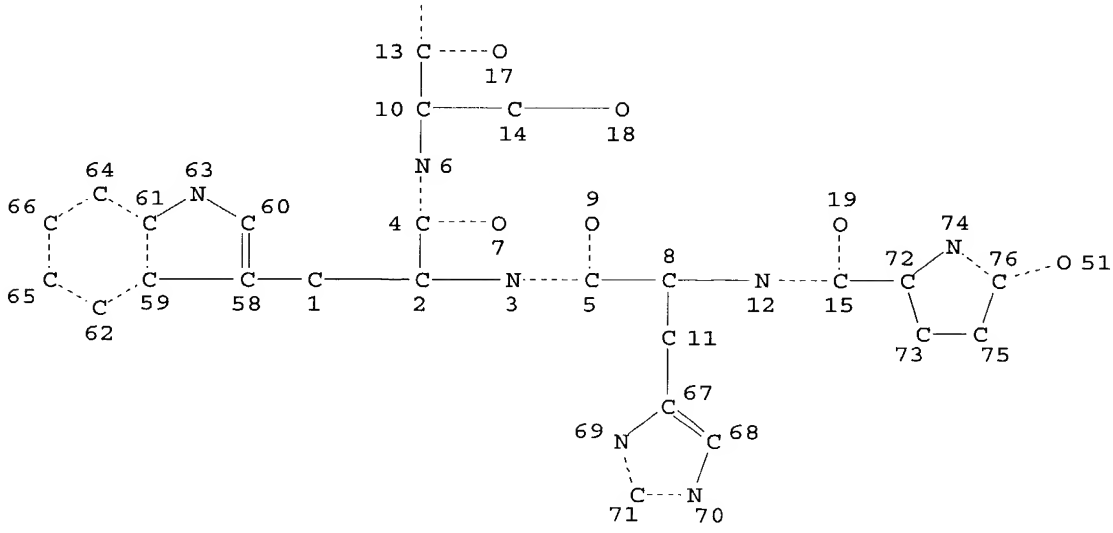

Page 3-A
NODE ATTRIBUTES:
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 83

STEREO ATTRIBUTES: NONE
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L7 (22) SEA FILE=REGISTRY ABB=ON PLU=ON L6 AND D
L8 22 SEA FILE=REGISTRY ABB=ON PLU=ON L7 AND D(3S) (LEU OR LEUCINE)

=> d que l9; d l9
L9 1 SEA FILE=REGISTRY ABB=ON PLU=ON 74381-53-6

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **74381-53-6** REGISTRY
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Luteinizing hormone-releasing factor (pig), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, monoacetate (salt)
OTHER NAMES:
CN Carcinil
CN Depo-Lupron
CN Enantone
CN Enantone Depot
CN LA 2550
CN Leuplin
CN Leuplin depot
CN Leuprin
CN Leuprolide acetate
CN Leuprorelin acetate
CN Lucrin
CN Lucrin Depot
CN Lupron
CN Lupron Depot
CN Procren Depot
CN Procrin
CN Prostap
CN TAP 144
CN TAP 144SR
CN Uno-Enantone
CN Viadur
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . C2 H4 O2
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DIOGENES, EMBASE, IMSCOSEARCH, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Book; Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

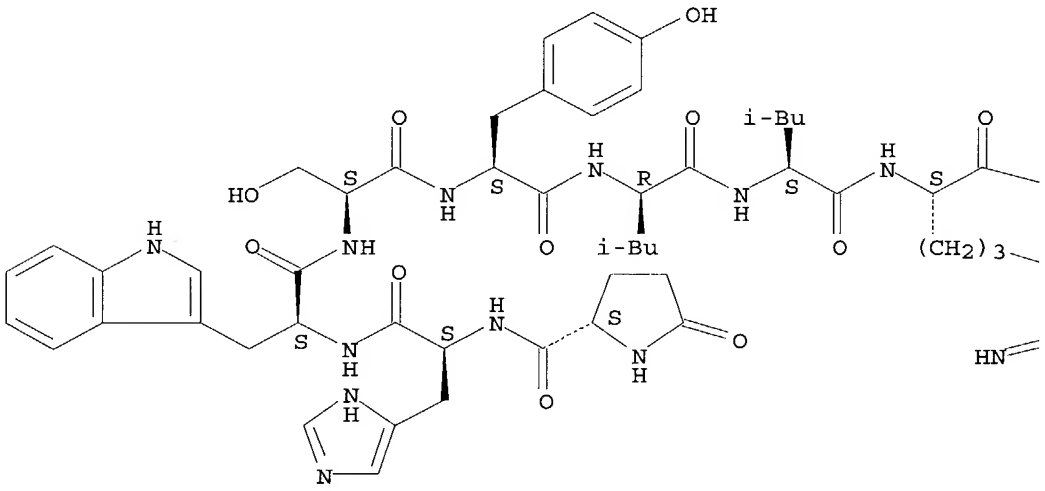
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

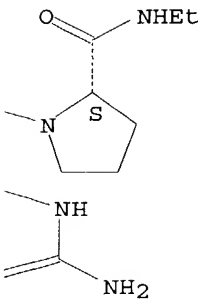
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



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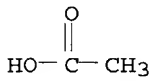
CRN 64-19-7
CMF C2 H4 O2



572 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
573 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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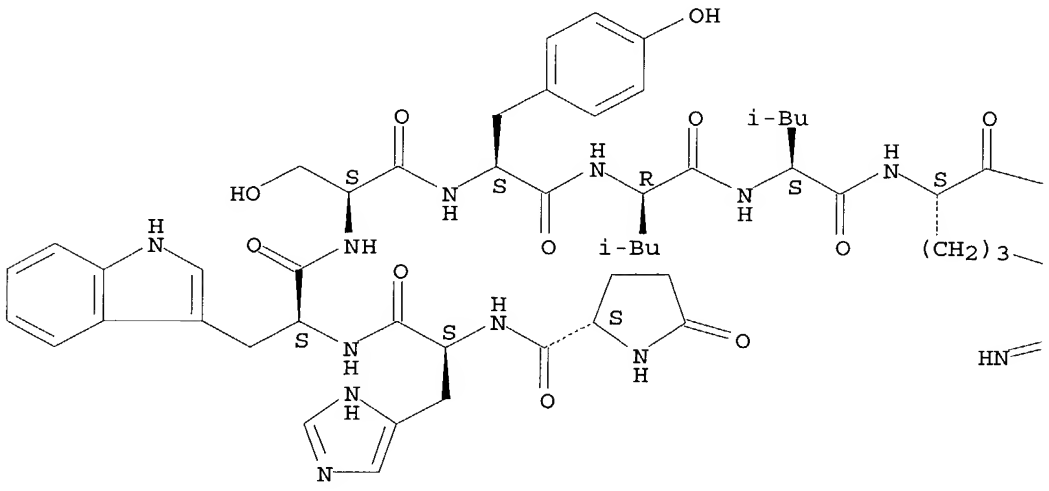
L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **53714-56-0** REGISTRY
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Luteinizing hormone-releasing factor (pig), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-
OTHER NAMES:
CN (D-Leu6, des-Gly-NH210)-LH-RH ethylamide
CN 1: PN: WO02087616 PAGE: 31 claimed protein
CN A 43818
CN D-Leu6-des-Gly10-LH-releasing hormone ethylamide
CN Des-Gly10-[D-Leu6]-LH-releasing hormone ethylamide
CN Des-Gly10-[D-Leu6]LH-RH ethylamide
CN Leuprolide
CN Leuprorelin
CN Lupron SR
CN NSC 377526
CN PGlu-His-Trp-Ser-Tyr-D-Leu-Leu-Arg-Pro-NHC2H5
FS PROTEIN SEQUENCE; STEREOSEARCH
DR 102586-10-7, 71873-71-7, 72648-87-4
MF C59 H84 N16 O12
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, TOXCENTER, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); PRP (Properties)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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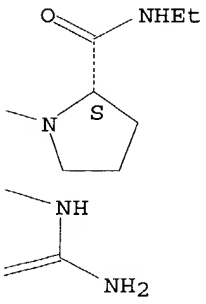

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664 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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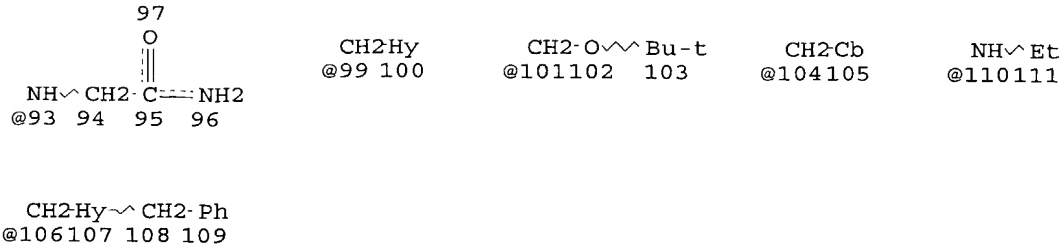
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CH2 Hy CH2 Ph
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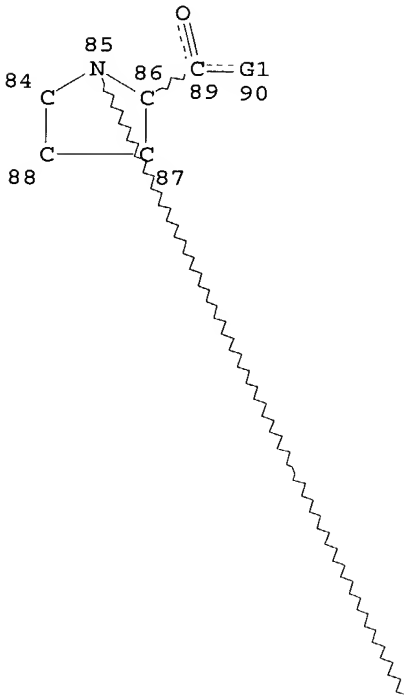
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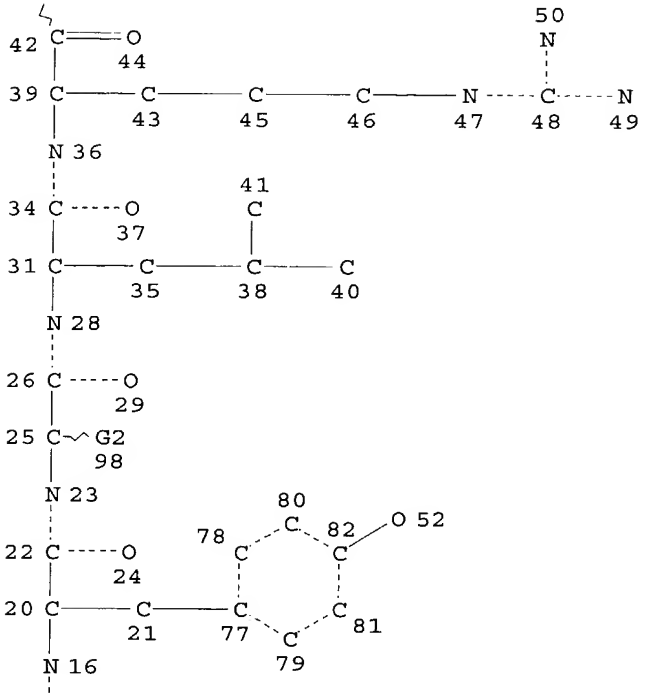
Page 2-A



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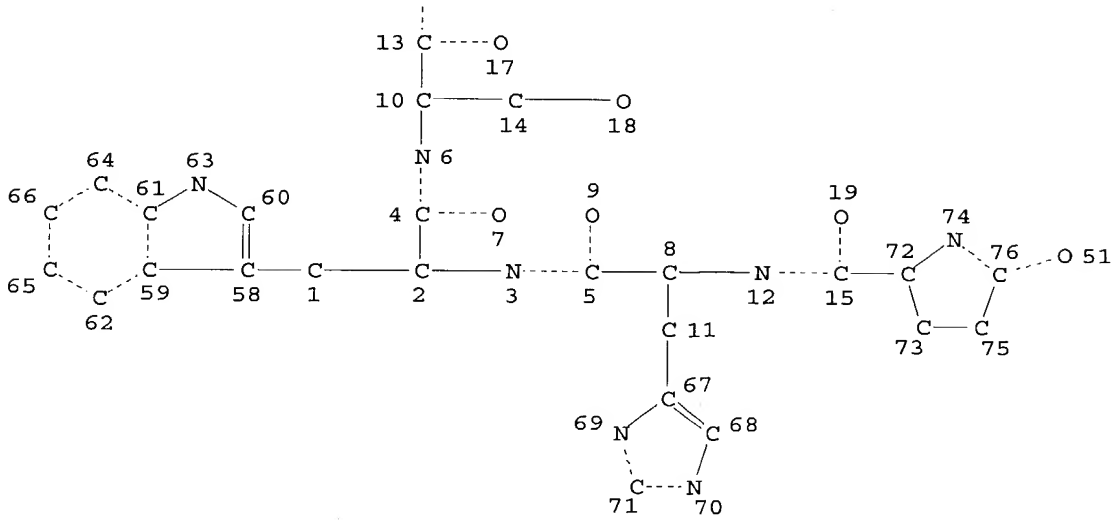

Page 4-A
VAR G1=110/93
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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS PCY UNS AT 100
GGCAT IS PCY UNS AT 105

GGCAT IS MCY UNS AT 107
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E8 C E1 N AT 100
ECOUNT IS E3 C E2 N AT 107

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 100

STEREO ATTRIBUTES: NONE
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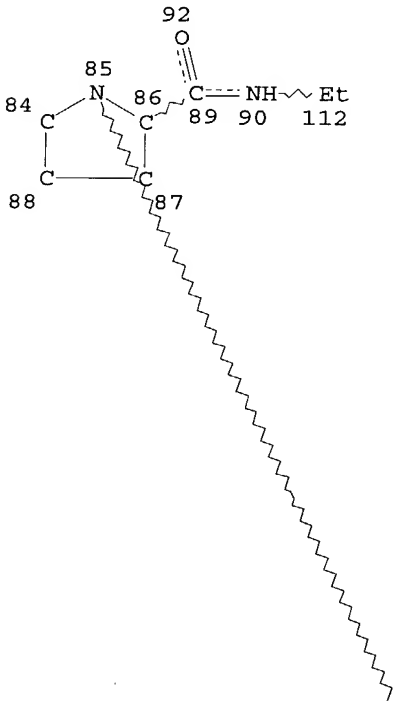

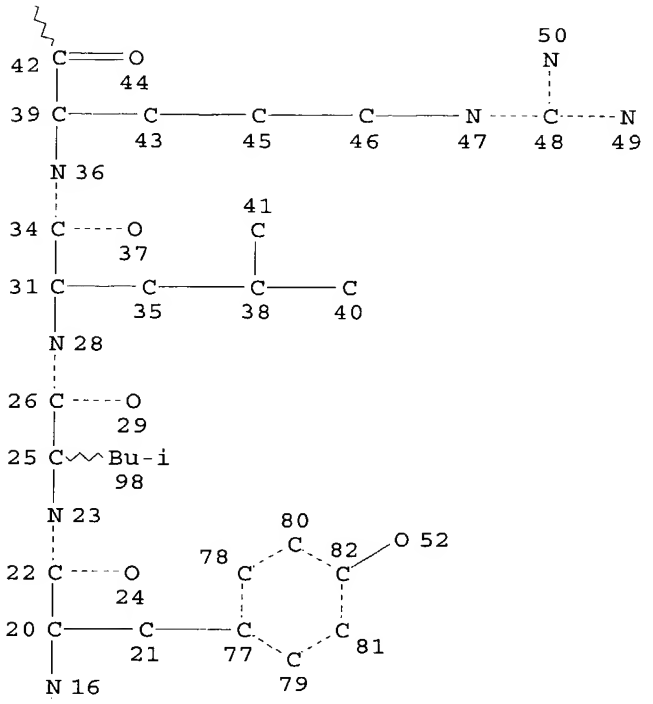

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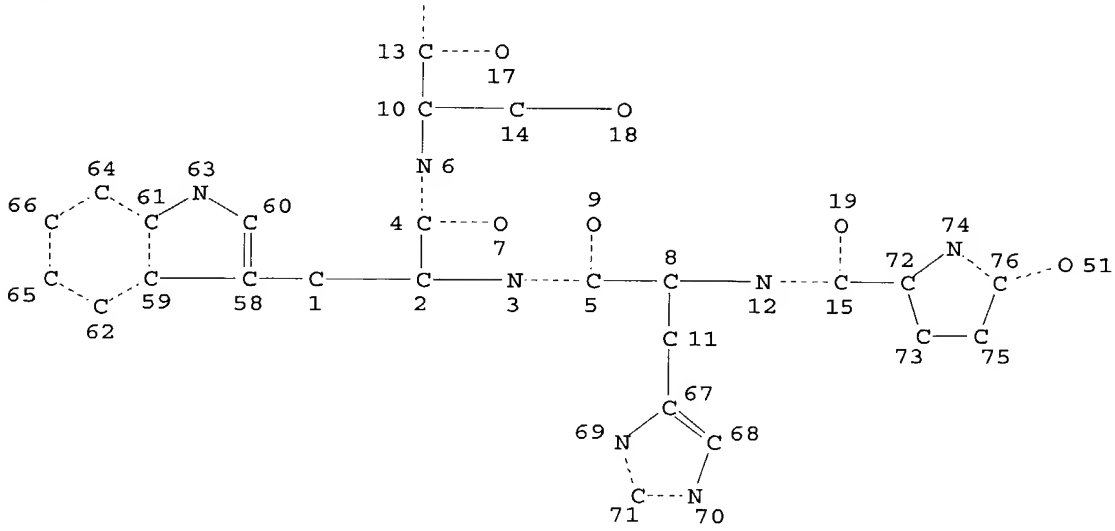

Page 3-A
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 83

STEREO ATTRIBUTES: NONE
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L7 (22) SEA FILE=REGISTRY ABB=ON PLU=ON L6 AND D
L8 22 SEA FILE=REGISTRY ABB=ON PLU=ON L7 AND D(3S) (LEU OR LEUCINE)
L9 1 SEA FILE=REGISTRY ABB=ON PLU=ON 74381-53-6
L10 1 SEA FILE=REGISTRY ABB=ON PLU=ON 53714-56-0
L11 20 SEA FILE=REGISTRY ABB=ON PLU=ON L8 NOT (L9 OR L10)

=> d l11 1-20 → L8 without sequence with too many hits.

L11 ANSWER 1 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 581088-28-0 REGISTRY
CN **1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, diacetate (salt) (9CI)** (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . 2 C2 H4 O2
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties); USES (Uses)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

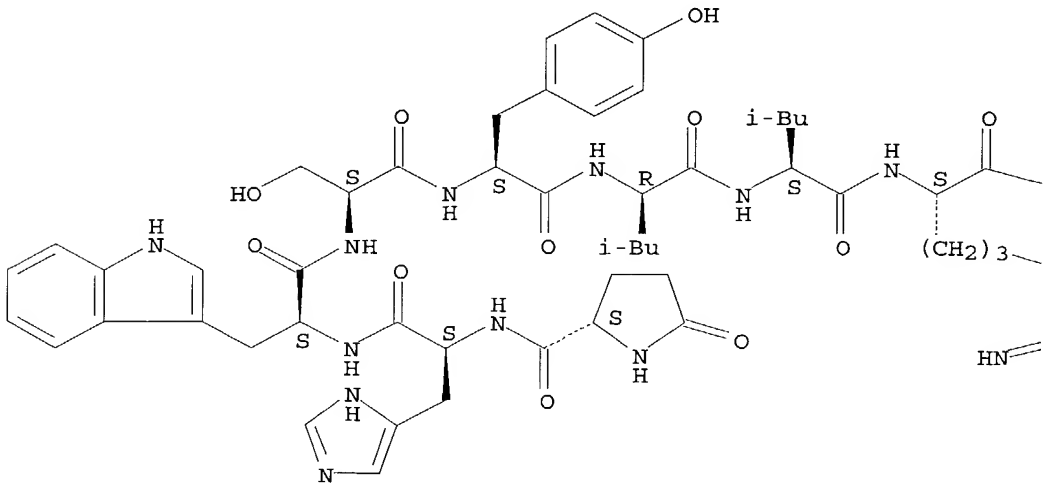
CM 1

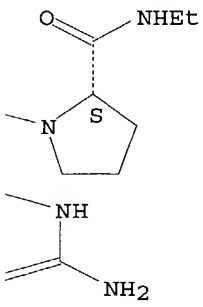
CRN 53714-56-0
CMF C59 H84 N16 O12

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A





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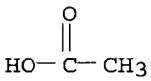


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 2 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 532959-44-7 REGISTRY
CN **1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, compd. with poly[oxy[(1R)-1-methyl-2-oxo-1,2-ethanediyl]] (9CI)** (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . x (C3 H4 O2)n
PCT Polyester
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation); PRP (Properties)

RELATED POLYMERS AVAILABLE WITH POLYLINK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

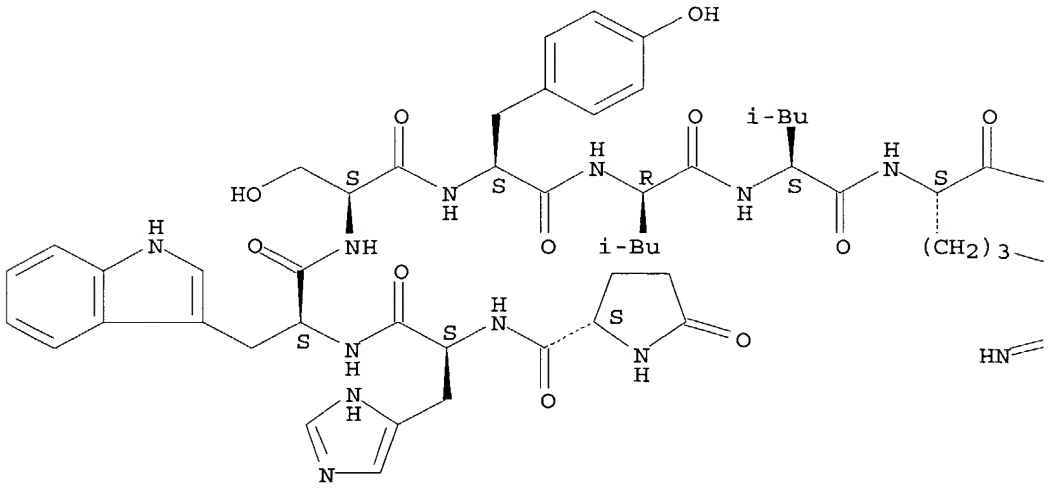
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

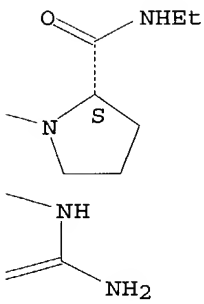
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A

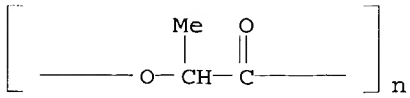


PAGE 1-B



CM 2

CRN 26917-25-9
CMF (C3 H4 O2)n
CCI PMS



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 3 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 532959-43-6 REGISTRY
CN **1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, compd. with (2R)-2-hydroxypropanoic acid homopolymer (9CI)** (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . x (C3 H6 O3)x
PCT Polyester, Polyester formed
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation); PRP (Properties)

RELATED POLYMERS AVAILABLE WITH POLYLINK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

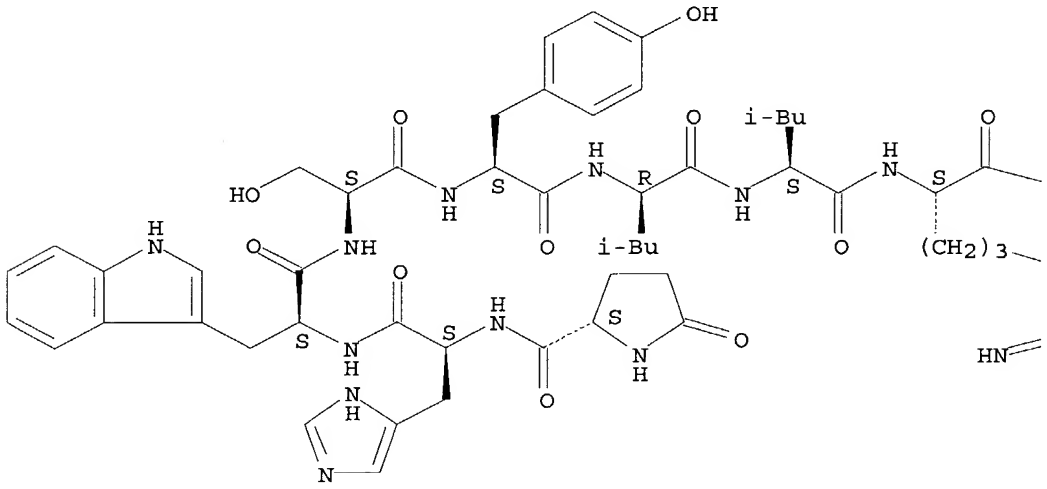
CM 1

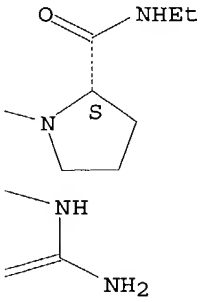
CRN 53714-56-0
CMF C59 H84 N16 O12

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A





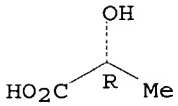
CM 2

CRN 106989-11-1
CMF (C3 H6 O3)x
CCI PMS

CM 3

CRN 10326-41-7
CMF C3 H6 O3

Absolute stereochemistry.



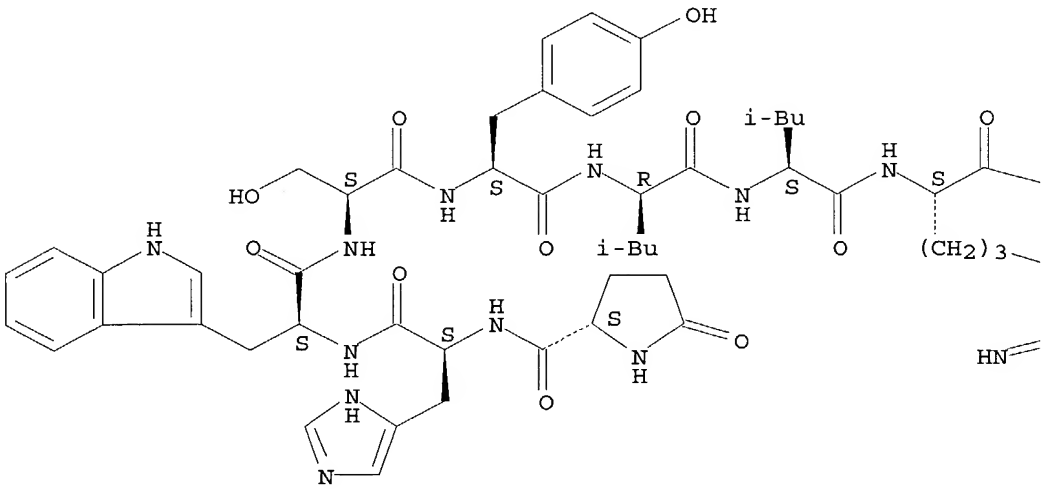
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 4 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 474787-24-1 REGISTRY
CN **1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monohydrochloride (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN 2: PN: WO02087616 PAGE: 31 claimed sequence
CN Leuprolide hydrochloride
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
CRN (53714-56-0)

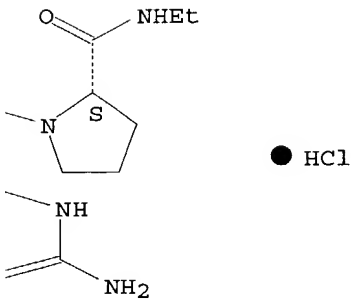
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 5 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 308811-89-4 REGISTRY
CN **1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, (9Z)-9-octadecenoate (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **9-Octadecenoic acid (9Z)-, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-1-9-luteinizing hormone-releasing factor (swine) (9CI)**
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . x C18 H34 O2
SR CA
LC STN Files: CA, CAPLUS

DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

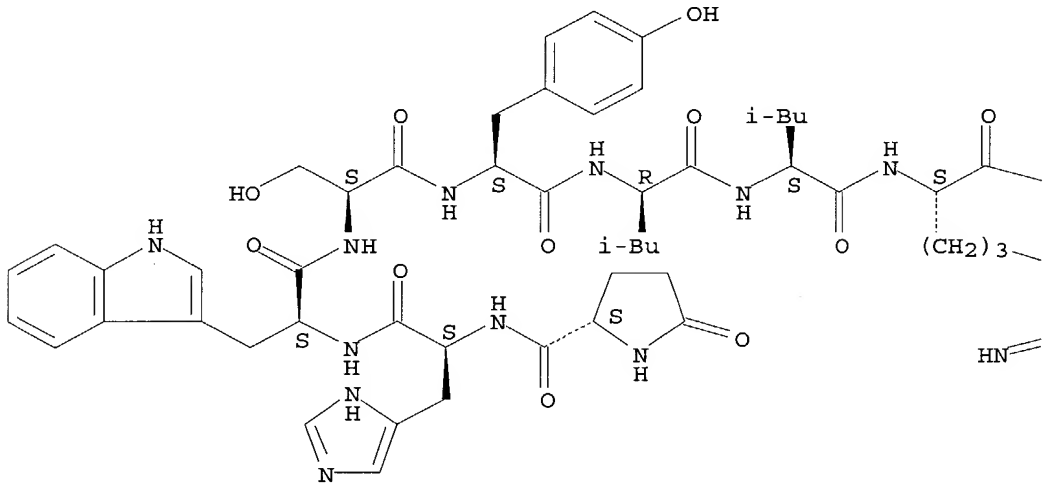
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

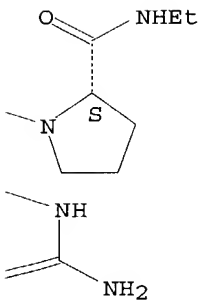
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A



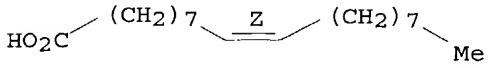
PAGE 1-B



CM 2

CRN 112-80-1
CMF C18 H34 O2

Double bond geometry as shown.



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 6 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 169047-57-8 REGISTRY
CN **Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, monohexadecanoate (salt) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Hexadecanoic acid, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (pig) (1:1)**
CN **Hexadecanoic acid, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (swine) (1:1) (9CI)**
CN **Luteinizing hormone-releasing factor (pig), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, monohexadecanoate (salt)**
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . C16 H32 O2
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

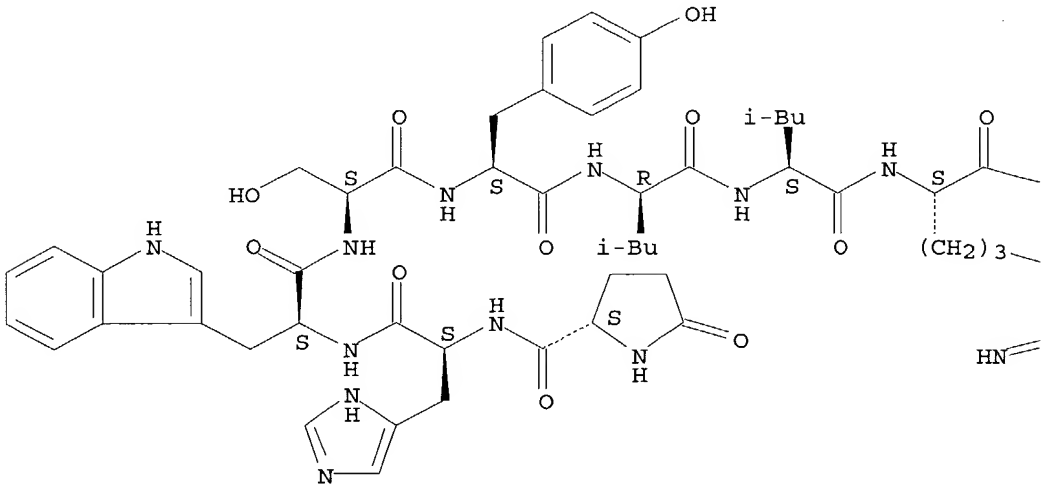
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

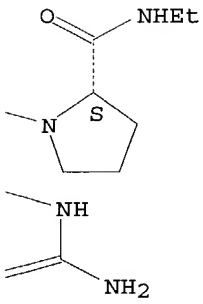
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



CM 2

CRN 57-10-3
CMF C16 H32 O2

$HO_2C-(CH_2)_{14}-Me$

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 7 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 153825-04-8 REGISTRY
CN **Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-**

L-prolinamide)-10-deglycinamide-, compd. with hydroxyoctadecanoic acid homopolymer (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Luteinizing hormone-releasing factor (pig), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, compd. with hydroxyoctadecanoic acid homopolymer**
CN **Octadecanoic acid, hydroxy-, homopolymer, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (pig)**
CN **Octadecanoic acid, hydroxy-, homopolymer, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (swine) (9CI)**
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . x (C18 H36 O3)x
PCT Polyester, Polyester formed
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

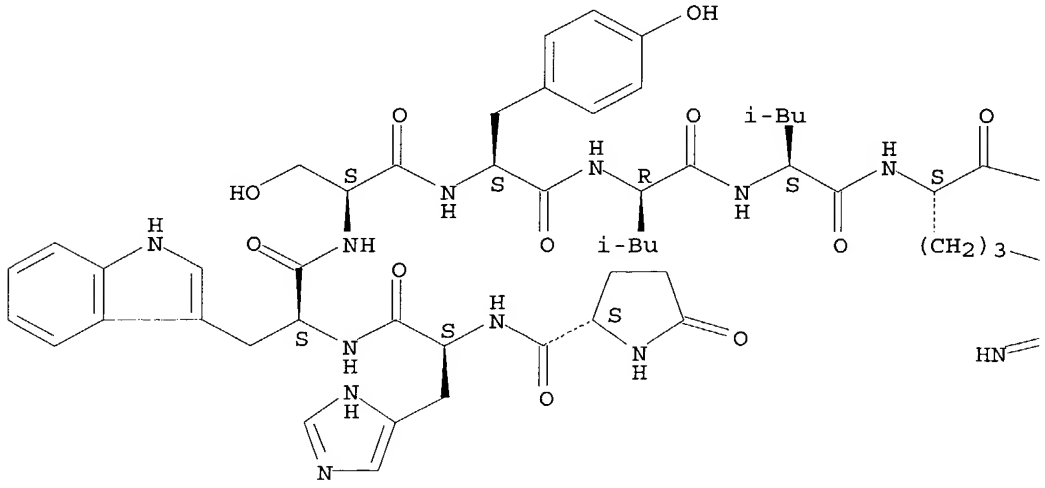
CM 1

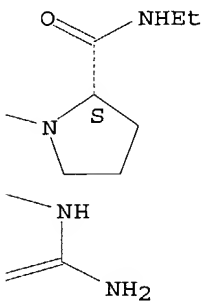
CRN 53714-56-0
CMF C59 H84 N16 O12

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A





CM 2

CRN 72006-34-9
CMF (C18 H36 O3)x
CCI PMS

CM 3

CRN 1330-70-7
CMF C18 H36 O3
CCI IDS

$HO_2C-(CH_2)_{16}-Me$

D1—OH

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 8 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 153724-53-9 REGISTRY
CN **Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, compd. with 3,6-dimethyl-1,4-dioxane-2,5-dione polymer with 1,4-dioxane-2,5-dione (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (swine) (9CI)**
CN **1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (pig)**
CN **1,4-Dioxane-2,5-dione, polymer with 3,6-dimethyl-1,4-dioxane-2,5-dione, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (pig) (9CI)**
CN **Luteinizing hormone-releasing factor (pig), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, compd. with 3,6-dimethyl-1,4-dioxane-2,5-**

dione polymer with 1,4-dioxane-2,5-dione

FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . x (C6 H8 O4 . C4 H4 O4)x
PCT Polyester, Polyester formed
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

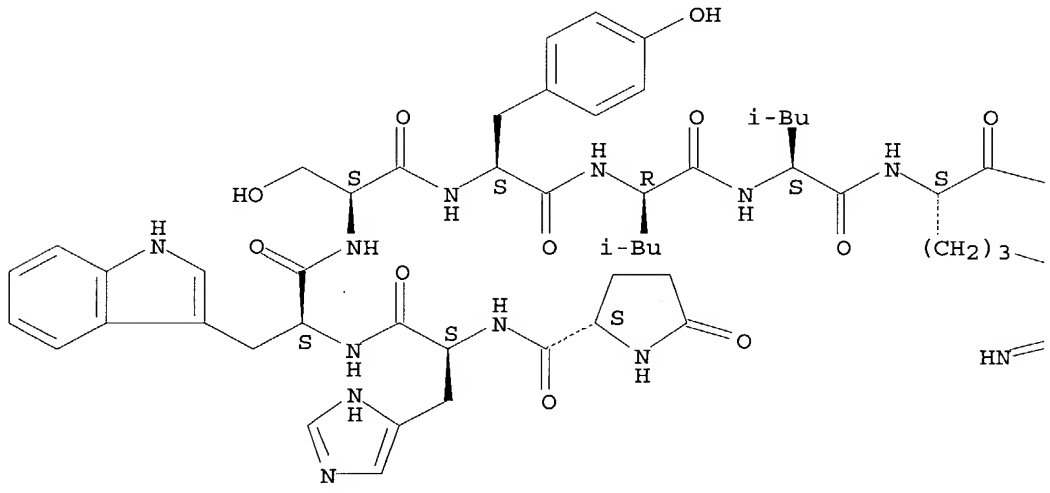
CM 1

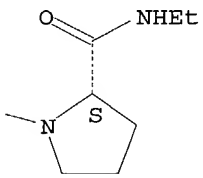
CRN 53714-56-0
CMF C59 H84 N16 O12

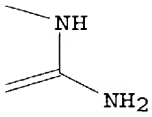
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A





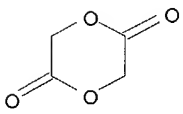


CM 2

CRN 26780-50-7
CMF (C6 H8 O4 . C4 H4 O4)x
CCI PMS

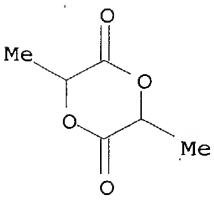
CM 3

CRN 502-97-6
CMF C4 H4 O4



CM 4

CRN 95-96-5
CMF C6 H8 O4



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 9 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 148352-41-4 REGISTRY

CN **Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, mono-1-octanesulfonate (salt) (9CI)** (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN **1-Octanesulfonic acid, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (pig) (1:1)**

CN **1-Octanesulfonic acid, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (swine) (1:1) (9CI)**

CN **Luteinizing hormone-releasing factor (pig), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, mono-1-octanesulfonate (salt)**

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C59 H84 N16 O12 . C8 H18 O3 S

SR CA

LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH

DT.CA CAplus document type: Journal

RL.NP Roles from non-patents: BIOL (Biological study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

CM 1

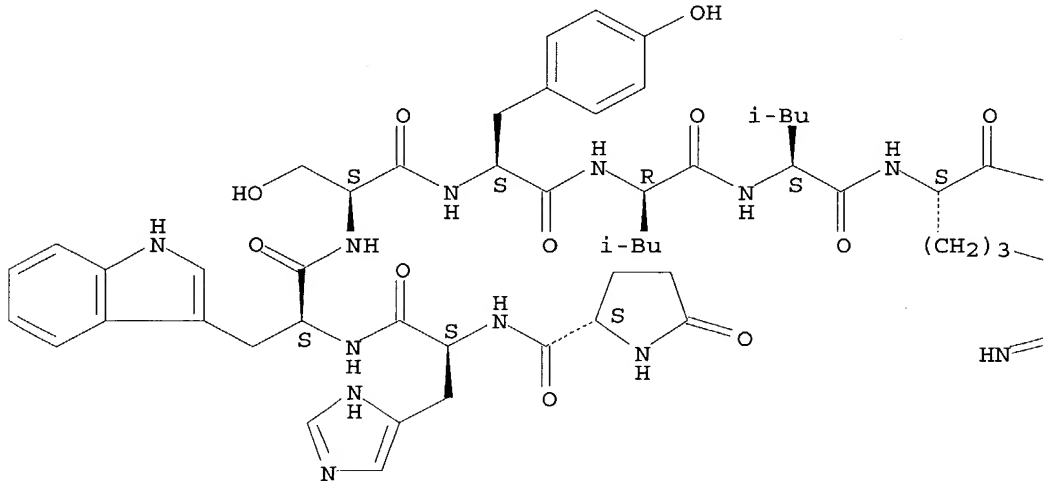
CRN 53714-56-0

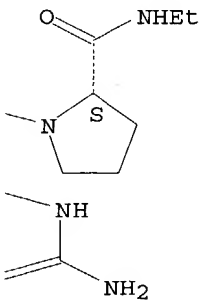
CMF C59 H84 N16 O12

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A





CM 2

CRN 3944-72-7
CMF C8 H18 O3 S

Me— $(CH_2)_7$ — SO_3H

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 10 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 148335-53-9 REGISTRY
CN **Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, mono-1-butanesulfonate (salt) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **1-Butanesulfonic acid, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (pig) (1:1)**
CN **1-Butanesulfonic acid, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (swine) (1:1) (9CI)**
CN **Luteinizing hormone-releasing factor (pig), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, mono-1-butanesulfonate (salt)**
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . C4 H10 O3 S
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

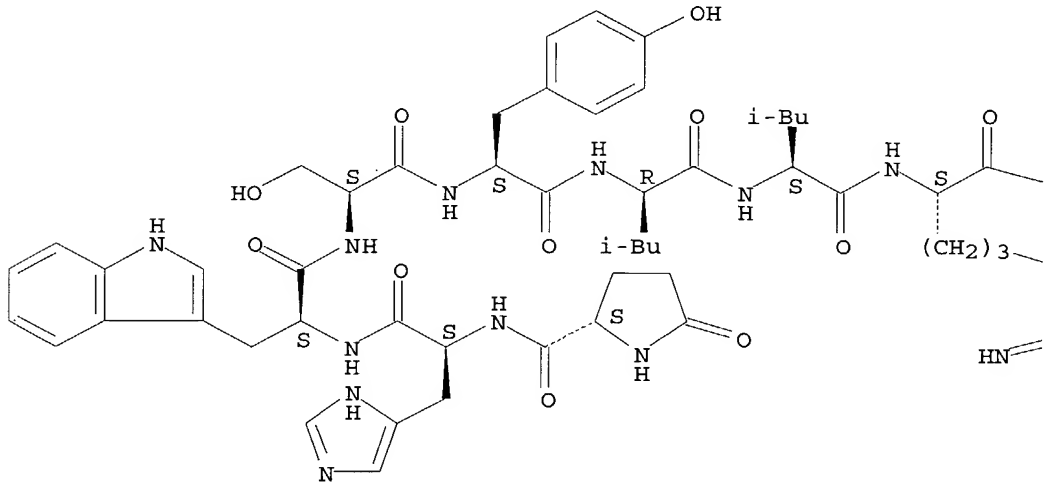
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

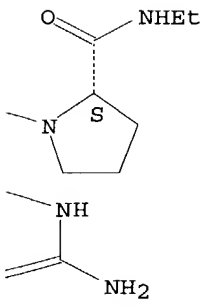
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A

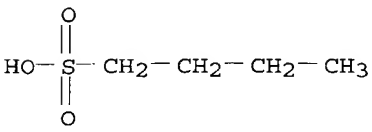


PAGE 1-B



CM 2

CRN 2386-47-2
CMF C4 H10 O3 S



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 11 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 148335-52-8 REGISTRY
CN **Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, mono-1-hexanesulfonate (1:1) (salt) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **1-Hexanesulfonic acid, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (pig) (1:1)**
CN **1-Hexanesulfonic acid, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (swine) (1:1) (9CI)**
CN **Luteinizing hormone-releasing factor (pig), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, 1-hexanesulfonate (1:1) (salt)**
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . C6 H14 O3 S
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

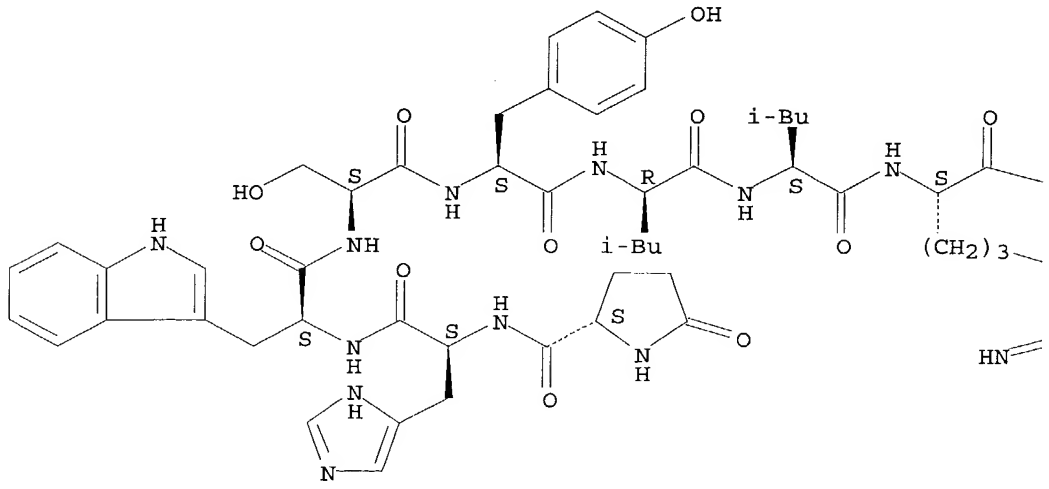
CM 1

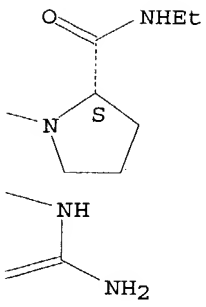
CRN 53714-56-0
CMF C59 H84 N16 O12

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A





CM 2

CRN 13595-73-8
CMF C6 H14 O3 S

Me— $(CH_2)_5$ — SO_3H

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 12 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 148335-51-7 REGISTRY
CN **Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, mono-1-decanesulfonate (salt) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **1-Decanesulfonic acid, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (pig) (1:1)**
CN **1-Decanesulfonic acid, compd. with 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamideluteinizing hormone-releasing factor (swine) (1:1) (9CI)**
CN **Luteinizing hormone-releasing factor (pig), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, mono-1-decanesulfonate (salt)**
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . C10 H22 O3 S
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

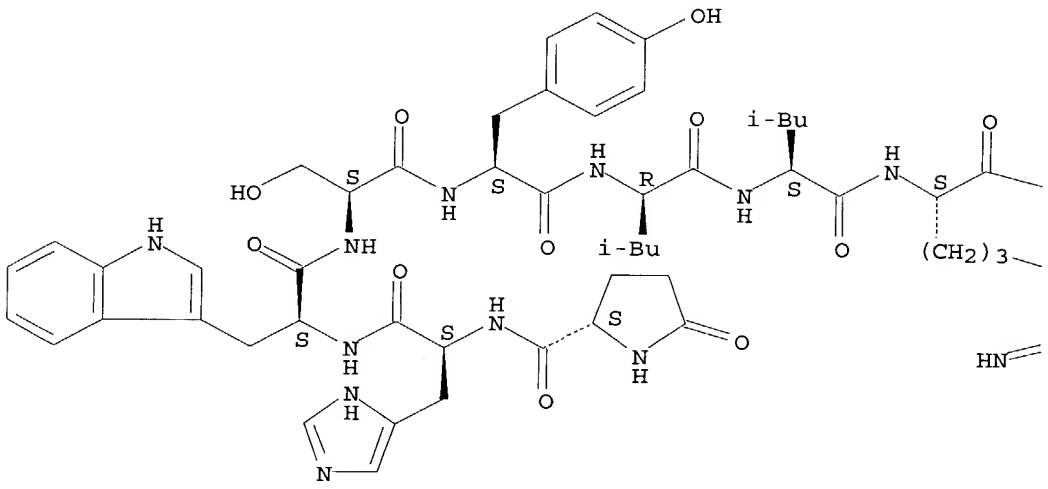
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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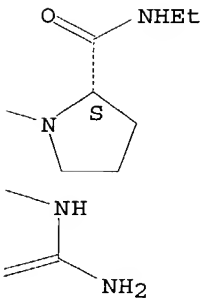


CM 2

CRN 20283-21-0
CMF C10 H22 O3 S

$HO_3S-(CH_2)_9-Me$

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

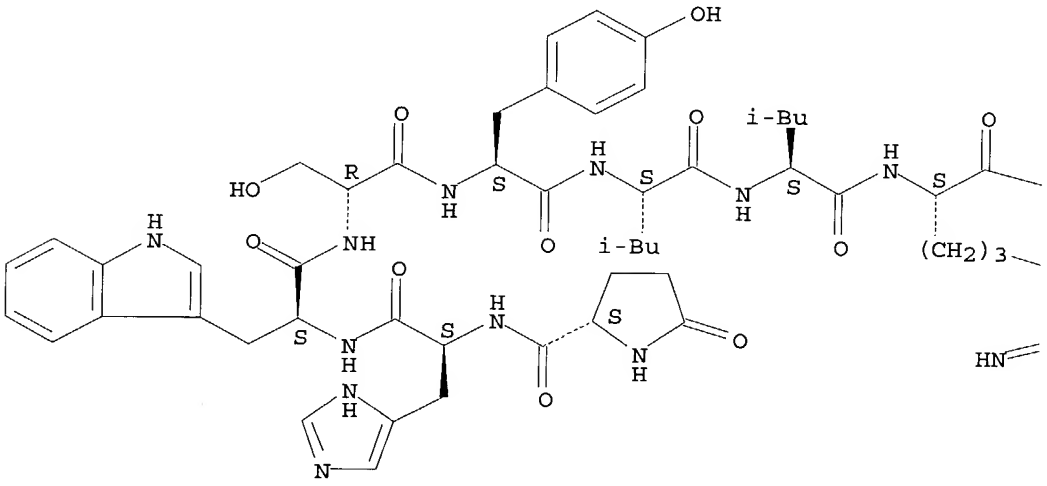
searched by Alex WaclawiwPage 35

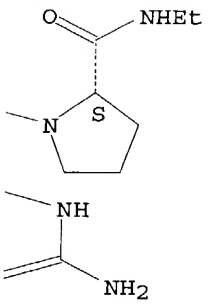
L11 ANSWER 13 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 112710-59-5 REGISTRY
CN **Luteinizing hormone-releasing factor (swine), 4-D-serine-6-L-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Luteinizing hormone-releasing factor (pig), 4-D-serine-6-L-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-**
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: ANST (Analytical study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A





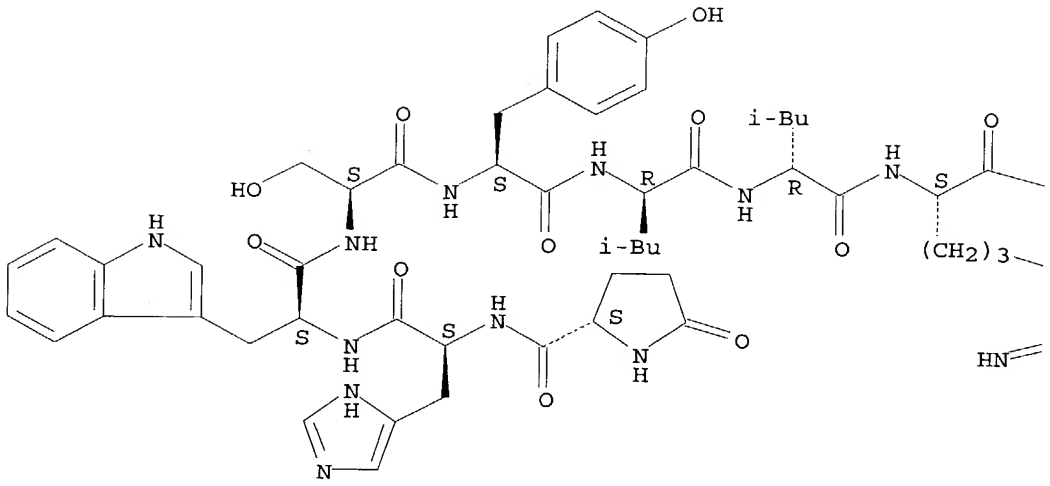
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 14 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 112710-58-4 REGISTRY
CN **Luteinizing hormone-releasing factor (swine), 6-D-leucine-7-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Luteinizing hormone-releasing factor (pig), 6-D-leucine-7-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-**
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: ANST (Analytical study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



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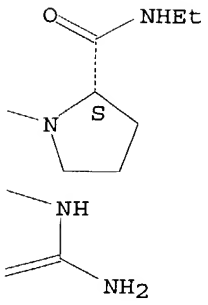

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 15 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 112710-57-3 REGISTRY
CN **Luteinizing hormone-releasing factor (swine), 5-D-tyrosine-6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Luteinizing hormone-releasing factor (pig), 5-D-tyrosine-6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-**
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS
(*File contains numerically searchable property data)

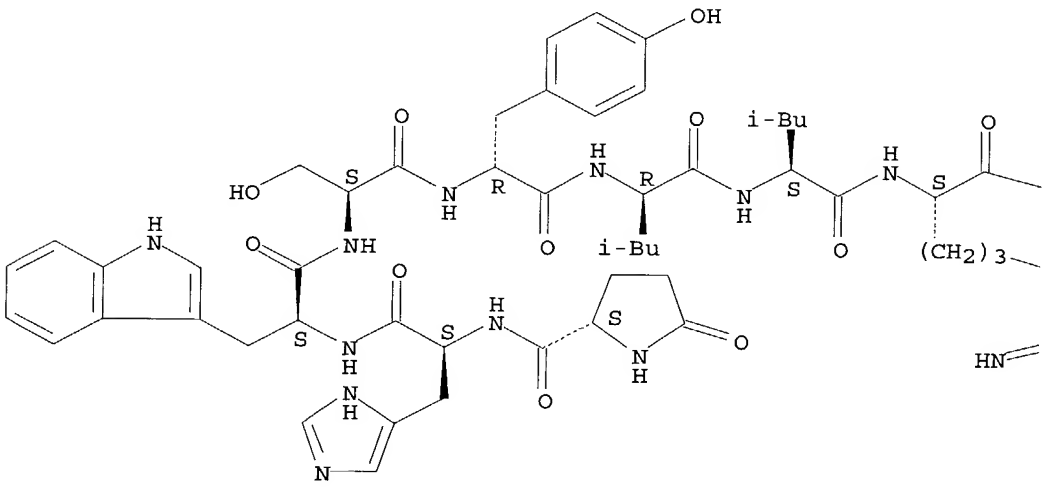
searched by Alex WaclawiwPage 38

DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: ANST (Analytical study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



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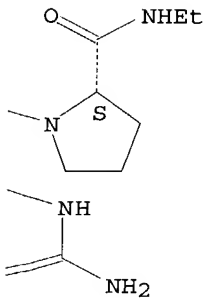


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

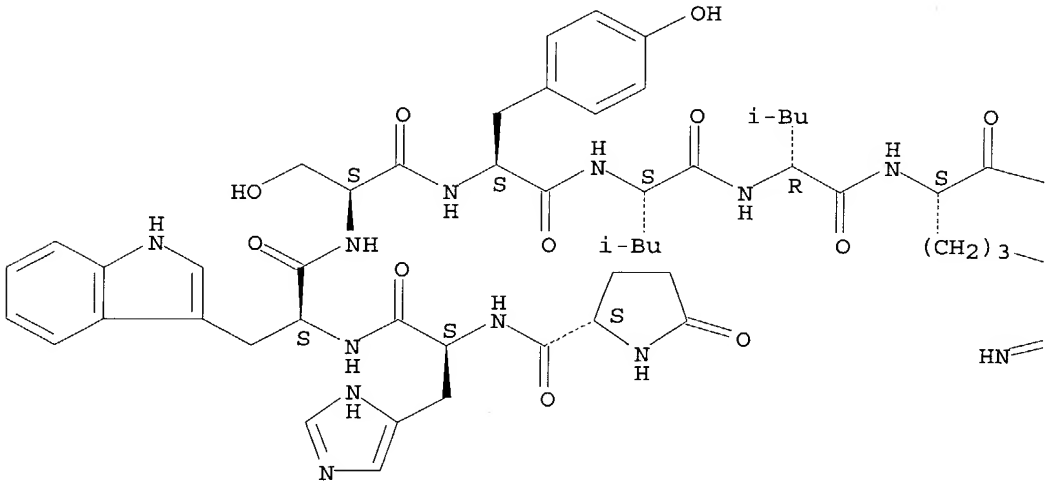
L11 ANSWER 16 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 112710-56-2 REGISTRY
CN **Luteinizing hormone-releasing factor (swine), 6-L-leucine-7-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Luteinizing hormone-releasing factor (pig), 6-L-leucine-7-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-**

FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: ANST (Analytical study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



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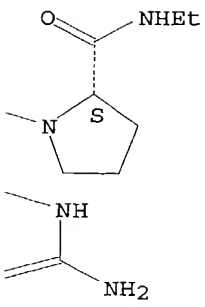


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

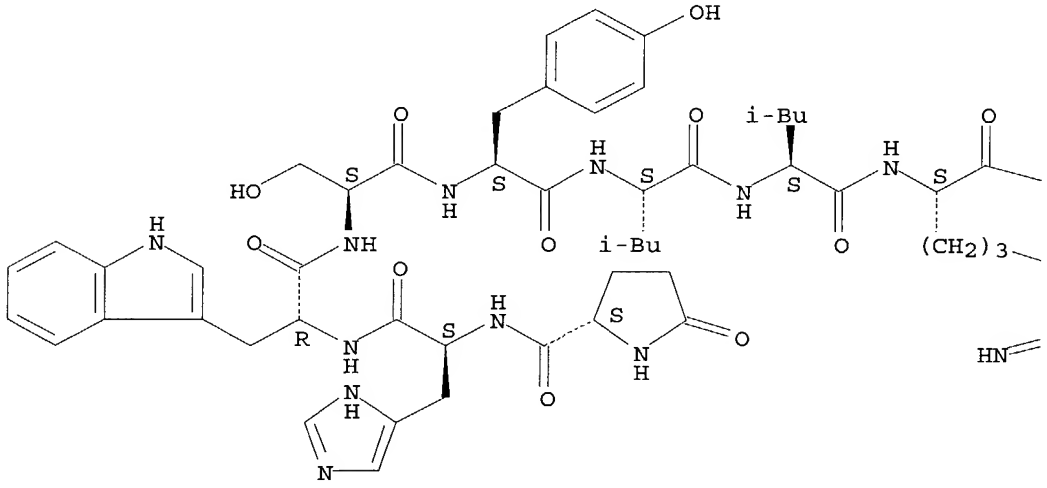
L11 ANSWER 17 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 112642-12-3 REGISTRY

CN **Luteinizing hormone-releasing factor (swine), 3-D-tryptophan-6-L-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Luteinizing hormone-releasing factor (pig), 3-D-tryptophan-6-L-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-**
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: ANST (Analytical study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



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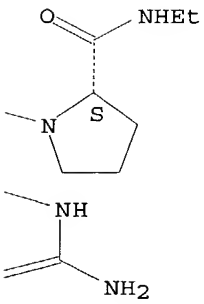


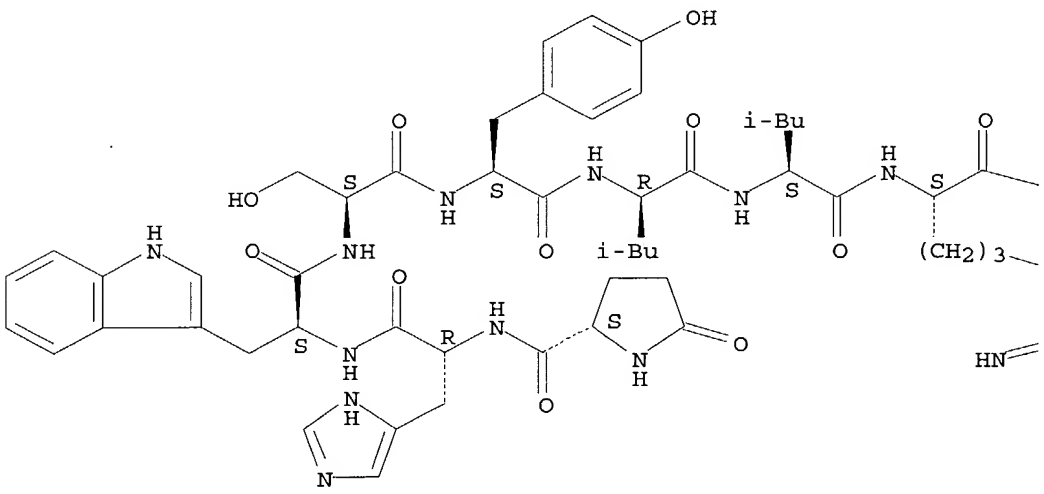
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

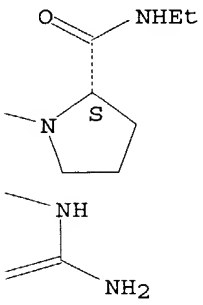
L11 ANSWER 18 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 112642-11-2 REGISTRY
CN **Luteinizing hormone-releasing factor (swine), 2-D-histidine-6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Luteinizing hormone-releasing factor (pig), 2-D-histidine-6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-**
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: ANST (Analytical study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A





1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 19 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN
RN 88793-81-1 REGISTRY
CN **1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, acetate (salt) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Luteinizing hormone-releasing factor (pig), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, acetate (salt)**
OTHER NAMES:
CN TAP-144 acetate
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12 . x C2 H4 O2
LC STN Files: BEILSTEIN*, CA, CAPLUS, IMSPATENTS, IMSRESEARCH, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PROC (Process); USES (Uses)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

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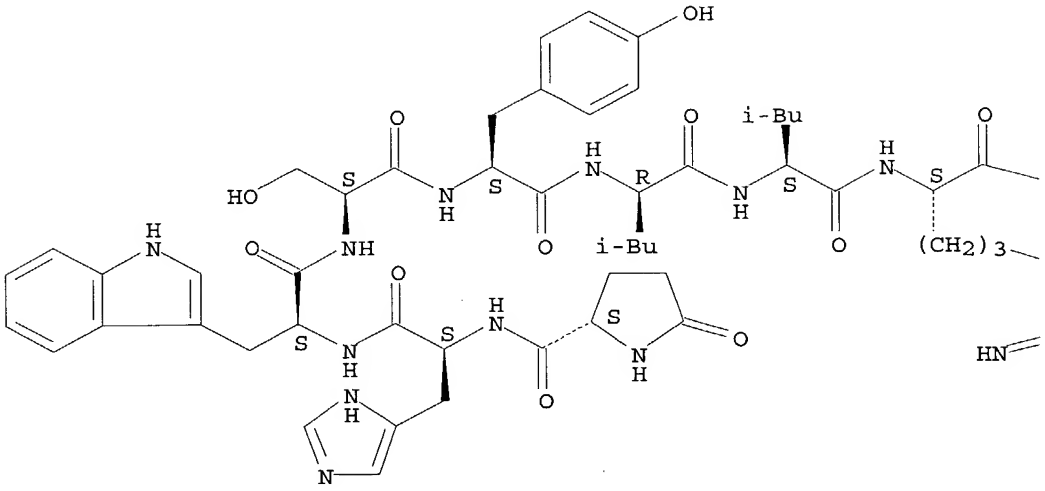
CRN 53714-56-0
CMF C59 H84 N16 O12

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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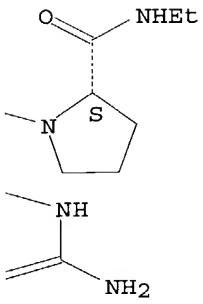
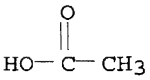


CM 2

CRN 64-19-7
CMF C2 H4 O2



2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

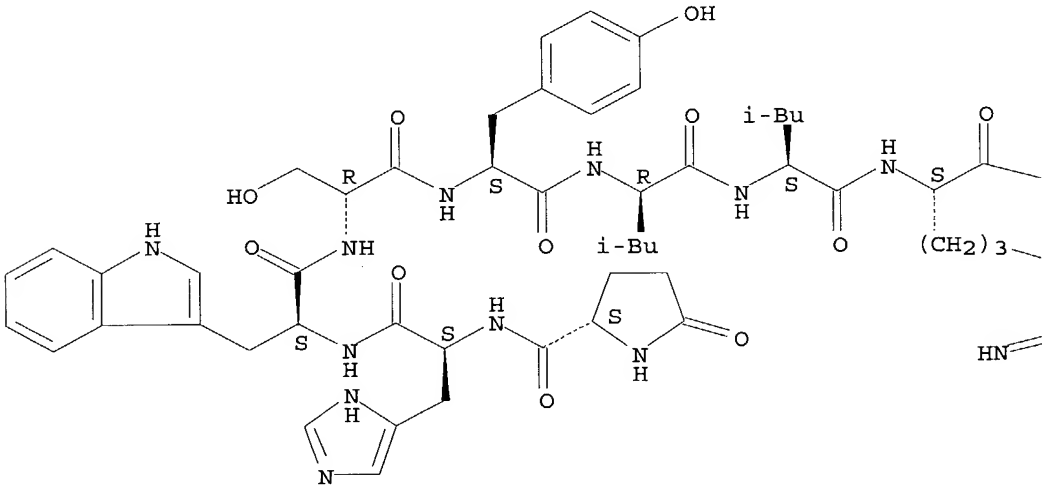
L11 ANSWER 20 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN

RN 62621-13-0 REGISTRY
CN **Luteinizing hormone-releasing factor (swine), 4-D-serine-6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Luteinizing hormone-releasing factor (pig), 4-D-serine-6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-**
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H84 N16 O12
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation)
RL.NP Roles from non-patents: BIOL (Biological study)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



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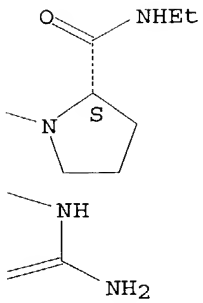

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 10 Jun 2004 VOL 140 ISS 24
FILE LAST UPDATED: 9 Jun 2004 (20040609/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d his l12-

L12 3640 S L2
L13 226 S L9 NOT (1999-2004)/PY
L14 312 S L10 NOT (1999-2004)/PY
L15 13 S L11

74381-53-6 and 53714-56-0 limited by date

=> d .ca hitstr l13 1-20;d .ca hitstr l14 1-20; d .ca hitstr l15 1-13

L13 ANSWER 1 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:180173 CAPLUS
DOCUMENT NUMBER: 131:843
TITLE: Intermittent complete androgen blockade in PSA relapse after radical prostatectomy and incidental prostate cancer
AUTHOR(S): Kurek, R.; Renneberg, H.; Lubben, G.; Kienle, E.; Tunn, Ulf W.
CORPORATE SOURCE: Urology Department, Offenbach Teaching Hospital, Offenbach, Germany
SOURCE: European Urology (1998), Volume Date 1999, 35(Suppl. 1), 27-31
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of this study was to determine the efficacy, safety and feasibility of intermittent androgen deprivation (IAD) in patients with prostate-specific antigen (PSA) relapse after radical prostatectomy or with an incidental prostate cancer (pT1B) after transurethral resection of

the prostate (TURP). Open, nonrandomized, prospective pilot study using the LH-releasing hormone analog (LH-RHa), leuprorelin acetate (1-mo depot) and cyproterone acetate. Forty-four patients have been enrolled. After a 30-64 mo' follow-up no progression to androgen-independent status has been observed Of the entire observation period, 26.6 mo (44-58%) remained treatment-free. During the treatment-free periods, normal testosterone levels were obtained, resulting in a cessation of the symptoms of androgen suppression and an improvement in quality of life. These results indicate that IAD is an effective and feasible therapy in patients with early stages of prostate cancer. Larger trials are necessary to confirm these encouraging results. Therefore, a European prospective, randomized, multicenter study (RE-LAPSE study) has been started to compare IAD with continuous androgen blockade in terms of time to tumor progression, safety and quality of life in patients with PSA relapse after radical prostatectomy.

CC 2-4 (Mammalian Hormones)

IT 427-51-0, Cyproterone acetate **74381-53-6**, Leuprorelin acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intermittent complete androgen blockade in PSA relapse after radical prostatectomy and incidental prostate cancer)

IT **74381-53-6**, Leuprorelin acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intermittent complete androgen blockade in PSA relapse after radical prostatectomy and incidental prostate cancer)

RN 74381-53-6 CAPLUS

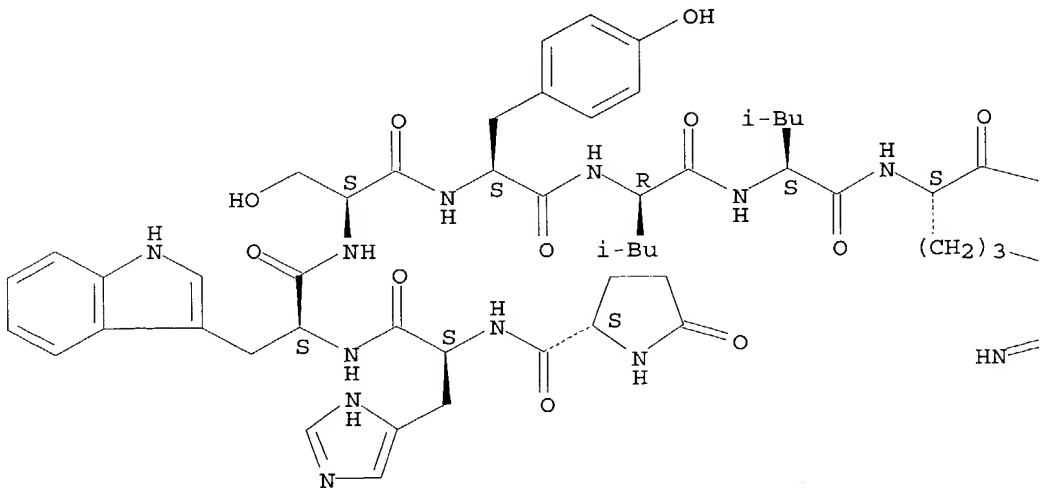
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

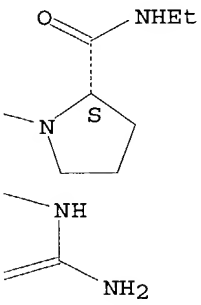
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

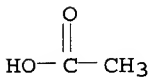
PAGE 1-A





CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:180171 CAPLUS
DOCUMENT NUMBER: 131:28093
TITLE: Role of neoadjuvant treatment in clinically confined prostate cancer
AUTHOR(S): Prezioso, Domenico; Lotti, Tullio; Montironi, Rodolfo; Polito, Mario
CORPORATE SOURCE: Clinica Urologica, Universita Federico II, Naples, I-80126, Italy
SOURCE: European Urology (1998), Volume Date 1999, 35(Suppl. 1), 17-22
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This prospective, randomized, multicenter comparative trial studied the effect of neoadjuvant hormonal treatment (NHT) prior to radical prostatectomy. Histopathol. tissue specimens were obtained from 91 consecutive patients (aged 60-70 yr) who underwent a radical prostatectomy for stage B prostate adenocarcinoma. The patients had received NHT for three months. Specimens were compared with those from 48 age-matched control patients who underwent similar surgery for stage B disease without receiving preoperative therapy. Treated tumors with an acinar pattern

were distinguishable from the untreated tumors by neoplastic acini that appeared shrunken and areas of individual infiltrating tumor cells separated by an abundant interglandular connective tissue. The epithelial tumor cells had inconspicuous nucleoli, nuclear shrinkage, chromatin condensation and pyknosis, cytoplasmic clearing, and enlargement by coalescence of vacuoles and rupture of cell membranes. No mitotic figures were seen in any treated tumors. Preliminary results show a benefit for patients receiving NHT in regard to the histol. indicators that we evaluated.

CC 2-4 (Mammalian Hormones)

IT 427-51-0, Cyproterone acetate **74381-53-6**, Leuprorelin acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of neoadjuvant treatment prior to radical prostatectomy in clin. confined prostate cancer)

IT **74381-53-6**, Leuprorelin acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of neoadjuvant treatment prior to radical prostatectomy in clin. confined prostate cancer)

RN 74381-53-6 CAPLUS

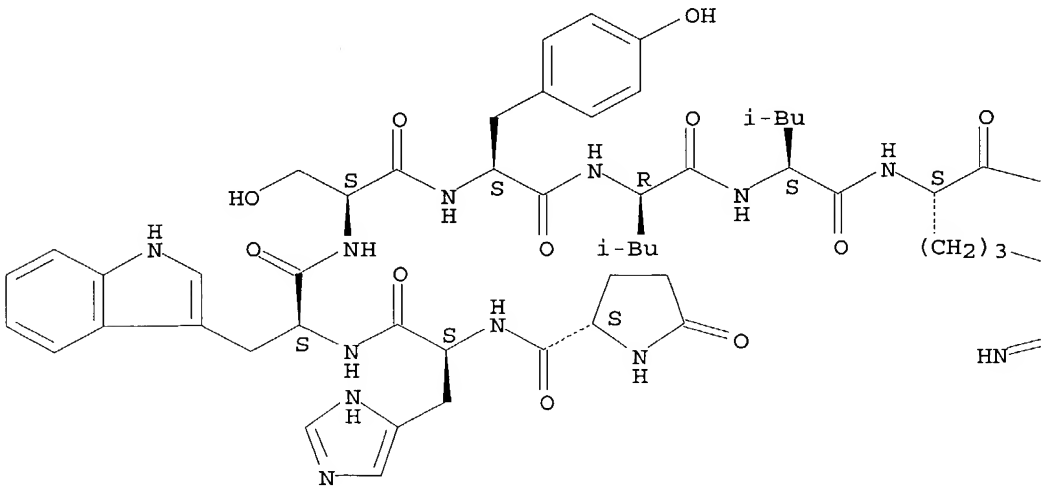
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

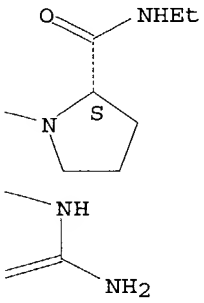
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

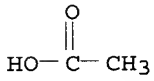
PAGE 1-A





CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:180170 CAPLUS
DOCUMENT NUMBER: 131:895
TITLE: Effect of leuprorelin acetate on cell growth and prostate-specific antigen gene expression in human prostatic cancer cells
AUTHOR(S): Sica, Gigliola; Iacopino, Fortunata; Settesoldi, Daniela; Zelano, Giovanni
CORPORATE SOURCE: Instituto di Istologia ed Embriologia, Facolta di Medicina e Chirurgia, Universita Cattolica del S. Cuore, Rome, I-00168, Italy
SOURCE: European Urology (1998), Volume Date 1999, 35(Suppl. 1), 2-8
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors investigated modulation of cell growth and prostate-specific antigen (PSA) gene expression in prostatic cancer cells by the LH-releasing hormone analog (LH-RHa), leuprorelin acetate, alone or combined with other agents. The effect of the analog on proliferation of both androgen-sensitive and -insensitive prostate cancer cells, maintained in different culture conditions, was evaluated by cell counts at various intervals of time. Basal expression of PSA gene and its variations were determined by a reverse transcriptase-polymerase chain reaction assay. LH-RHa is ineffective in regulating cell growth, when used alone in both

hormone-sensitive and -insensitive cell lines. Nevertheless, it counteracts the stimulatory action of androgens on proliferation of LNCaP cells, which respond to low concns. of dihydrotestosterone. Moreover, LH-RHa has an inhibitory effect on the mitogenic action of epidermal growth factor (EGF) in androgen-unresponsive PC-3 cells. The analog reduces PSA gene expression in both hormone-sensitive and -insensitive cells. Interestingly, it counteracts the gene expression induced by androgens in LNCaP cells and by EGF in PC-3 cells. These data show that LH-RHa may behave like a neg. growth factor, which directly regulates cell growth and PSA gene expression. Moreover, the authors' findings support the idea that growth factors may interfere with the androgen signaling pathway.

CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 14

IT **74381-53-6**, Leuprorelin acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leuprorelin acetate effect on cell growth and prostate-specific antigen gene expression in human androgen-sensitive and androgen-insensitive prostatic cancer cells)

IT **74381-53-6**, Leuprorelin acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leuprorelin acetate effect on cell growth and prostate-specific antigen gene expression in human androgen-sensitive and androgen-insensitive prostatic cancer cells)

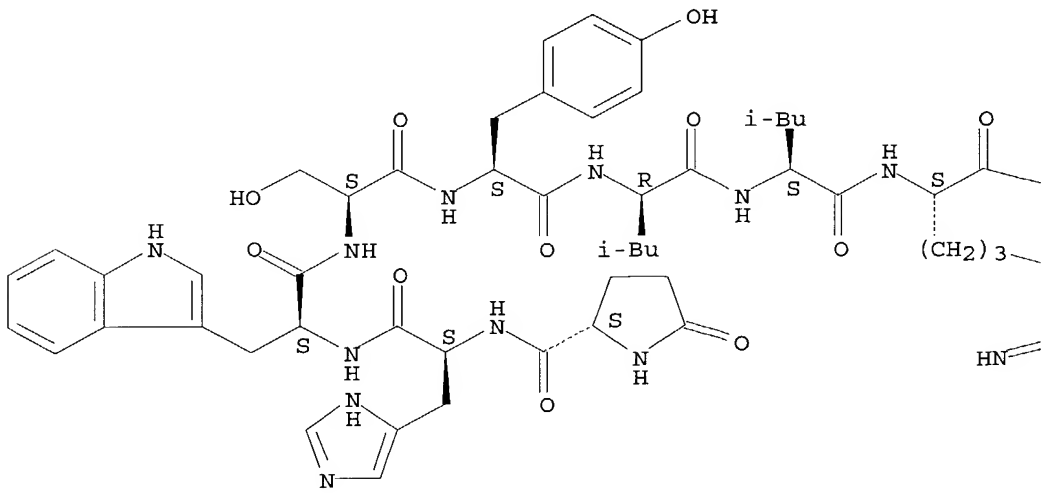
RN 74381-53-6 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

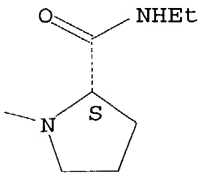
CM 1

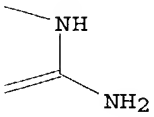
CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A

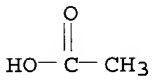






CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:51770 CAPLUS
DOCUMENT NUMBER: 130:247151
TITLE: Ovarian hyperstimulation following the sole administration of agonistic analogs of gonadotropin releasing hormone
AUTHOR(S): Weissman, Ariel; Barash, Amihai; Shapiro, Heather; Casper, Robert F.
CORPORATE SOURCE: Division of Reproductive Sciences, Department of Obstetrics and Gynecology, The Toronto Hospital, University of Toronto, Toronto, ON, M5G 2C4, Can.
SOURCE: Human Reproduction (1998), 13(12), 3421-3424
CODEN: HUREEE; ISSN: 0268-1161
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ovarian hyperstimulation following the sole administration of gonadotropin-releasing hormone agonists (GnRHa) is exceedingly rare. We hereby report on two infertile patients undergoing in-vitro fertilization-embryo transfer who developed ovarian hyperstimulation under such circumstances. In both patients, GnRHa were administered using the "long protocol" regimen. The first patient developed ovarian hyperstimulation on two occasions, with mid-luteal depot administration of

triptorelin and with early follicular triptorelin, administered as daily s.c. injections. In both cycles, within 2 wk of triptorelin therapy, massive ovarian multifollicular enlargement occurred, concomitant with high serum estradiol concns., which resolved spontaneously following expectant management. The second patient developed ovarian hyperstimulation following daily injections of leuprolide acetate starting at the mid-luteal phase. The final stage of ovulation was triggered by human chorionic gonadotropin (HCG) and 11 oocytes were retrieved. In-vitro fertilization resulted in embryo formation, but failed to result in pregnancy. The same phenomenon recurred in a subsequent cycle despite preventive pretreatment with an oral contraceptive. A neg. GnRH test, performed just before HCG administration, suggested than an ongoing "flare-up effect" was unlikely to cause ovarian stimulation. Ovarian hyperstimulation can occur following the sole administration of GnRHa irresp. of the preparation used and the administration protocol. Although spontaneous resolution is the rule, once this condition has developed, HCG administration and oocyte retrieval are feasible. This rare entity probably represents an exaggerated form of ovarian cyst formation following GnRHa administration, the underlying pathophysiol. of which remains unresolved.

CC 2-3 (Mammalian Hormones)

IT 57773-63-4, Triptorelin **74381-53-6**, Leuprolide acetate
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovarian hyperstimulation following sole administration of LH-RH agonists in women)

IT **74381-53-6**, Leuprolide acetate
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovarian hyperstimulation following sole administration of LH-RH agonists in women)

RN 74381-53-6 CAPLUS

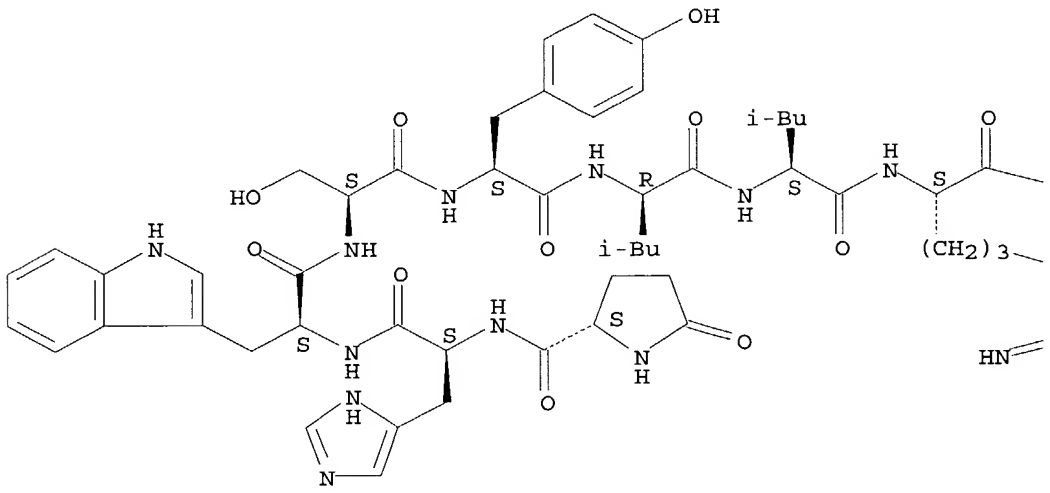
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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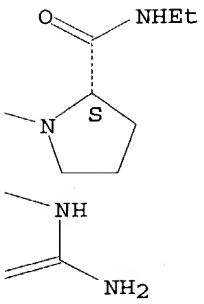

CM 2

CRN 64-19-7
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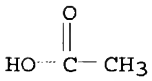


REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN

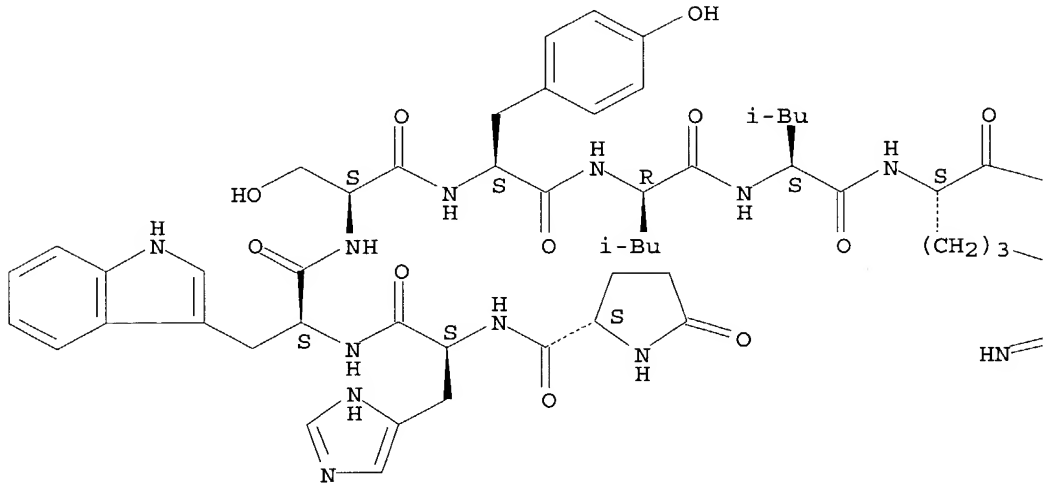
ACCESSION NUMBER: 1999:51756 CAPLUS
DOCUMENT NUMBER: 130:247148
TITLE: Human chorionic gonadotropin luteal support overcomes luteal phase inadequacy after gonadotropin-releasing hormone agonist-induced ovulation in gonadotropin-stimulated cycles
AUTHOR(S): Penarrubia, Joana; Balasch, Juan; Fabregues, Francisco; Creus, Montserrat; Casamitjana, Roser; Ballesca, Jose; Puerto, Bienvenido; Vanrell, Juan A.
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Faculty of Medicine-University of Barcelona, Barcelona, Spain
SOURCE: Human Reproduction (1998), 13(12), 3315-3318
CODEN: HUREEE; ISSN: 0268-1161
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Gonadotropin-releasing hormone agonist (GnRHa)-induced ovulation after gonadotropin ovarian stimulation is used to prevent ovarian hyperstimulation syndrome and multiple pregnancy in polyfollicular cycles. However, one of the major problems to be resolved is corpus luteum function after follicular maturation and ovulation by mid-cycle GnRHa administration. The present report investigated the luteal phase in non-conceptual polyfollicular cycles in 26 patients (group 1) receiving a single dose of 0.5 mg leuprolide acetate to induce ovulation and in a control group of patients (n = 26) (group 2) who were given human chorionic gonadotropin (HCG) (10 000 IU, i.m.) for ovulation induction. All of them were normal ovulatory women undergoing gonadotropin ovarian stimulation because of unexplained infertility or male factor. In both groups of patients two doses of 2500 IU HCG i.m. were given 6 and 10 days after the ovulatory dose of HCG or GnRHa to support the luteal phase. All cycles were ovulatory as shown by mid-luteal serum progesterone concns. >10 ng/mL. Mean serum progesterone concns. were 62% higher in group 2 than in group 1, but this difference was not statistically significant. The mean length of the luteal phase was similar in groups 1 and 2. It is concluded that HCG luteal support is a useful tool to overcome the luteal phase inadequacy that characterizes GnRHa-triggered cycles after gonadotropin stimulation.
CC 2-3 (Mammalian Hormones)
IT 9002-61-3, Chorionic gonadotropin **74381-53-6**, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human chorionic gonadotropin luteal support for progesterone secretion overcomes luteal phase inadequacy after LH-RH agonist-induced ovulation in gonadotropin-stimulated cycles)
IT **74381-53-6**, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human chorionic gonadotropin luteal support for progesterone secretion overcomes luteal phase inadequacy after LH-RH agonist-induced ovulation in gonadotropin-stimulated cycles)
RN 74381-53-6 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

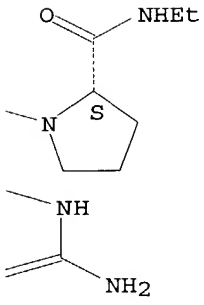
CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A

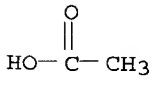


PAGE 1-B



CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:785345 CAPLUS
DOCUMENT NUMBER: 130:134499
TITLE: Leuprolide, a gonadotropin-releasing hormone agonist, enhances colonization after spermatogonial transplantation into mouse testes
AUTHOR(S): Ogawa, T.; Dobrinski, I.; Avarbock, M. R.; Brinster, R. L.
CORPORATE SOURCE: School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA, 19104-6009, USA
SOURCE: Tissue & Cell (1998), 30(5), 583-588
CODEN: TICEBI; ISSN: 0040-8166
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Spermatogonial stem cells can be transplanted from a fertile donor mouse to the testis of an infertile recipient where they establish spermatogenesis and produce spermatozoa. In the present study we investigated whether treatment of recipient mice with the gonadotropin-releasing hormone (GnRH) agonist leuprolide acetate could alter the efficiency of colonization by donor spermatogonial stem cells in the recipient testis. Six recipient mice were treated with busulfan to destroy endogenous spermatogenesis followed by injection of leuprolide acetate to three of the mice. Testis cells from mice carrying the ZFIacZ transgene, which produces β-galactosidase in spermatids, were used as donor cells for transplantation to allow for identification of donor spermatogenesis in the recipient testis by staining for enzyme activity. The extent of donor cell colonization was compared between leuprolide treated recipients and untreated control mice 3 mo after transplantation. Efficiency of colonization by donor cells was markedly enhanced in recipient mice treated with the GnRH agonist leuprolide acetate, which makes the technique of spermatogonial transplantation applicable to a wide range of exptl. situations. The present study also indicates that this technique can be used as a biol. assay system to investigate factors controlling the establishment and progression of spermatogenesis.

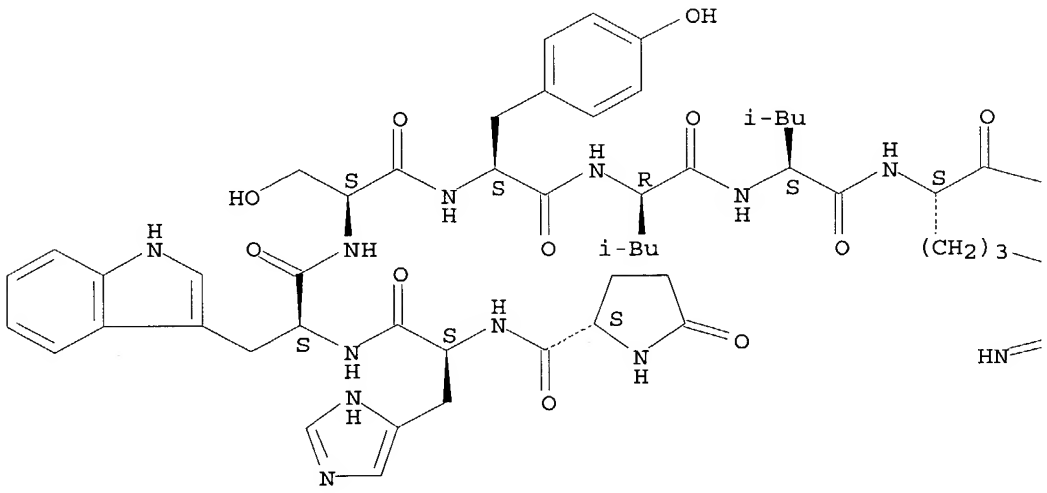
CC 2-10 (Mammalian Hormones)
IT 53714-56-0, Leuprolide **74381-53-6**, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(leuprolide enhances colonization after spermatogonial transplantation into mouse testes)
IT **74381-53-6**, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(leuprolide enhances colonization after spermatogonial transplantation into mouse testes)
RN 74381-53-6 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

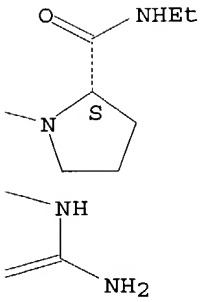
CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



CM 2

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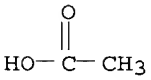


REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:774690 CAPLUS
DOCUMENT NUMBER: 130:33265
TITLE: Evaluation of ovarian cysts following GnRH-a treatment in patients with polycystic ovarian syndrome
AUTHOR(S): Gregoriou, O.; Vitoratos, N.; Konidaris, S.; Papadias, C.; Chryssikopoulos, A.
CORPORATE SOURCE: Second Dep. Obstetrics Gynecology, Areteion Hospital, Athens, 11528, Greece
SOURCE: Gynecologic and Obstetric Investigation (1998), 46(4), 252-255
CODEN: GOBIDS; ISSN: 0378-7346
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ovarian cysts which appeared during gonadotropin-releasing hormone analogs(GnRH-a)/human gonadotropins (hMG) treatment were evaluated in 35 women with polycystic ovarian syndrome. Women received 3.75 mg IM of long-acting leuprolide acetate on the 1st day of the menstrual cycle. In 15.5% of menstrual cycles, ovarian cysts with a diameter of ≥20 mm developed. The blood serum estradiol (E2) levels, were ≥35 and ≤35 pg/mL in 11 and 3 cases (group A and B), resp. Ovarian cysts in group A and B were 42 vs. 24.2 mm, resp. When the serum E2 concentration were ≤35 pg/mL, the ovarian cysts were disregarded and ovarian stimulation with hMG was initiated. When serum E2 levels were ≥35 pg/mL, the initiation of the ovarian stimulation with hMG was postponed until serum E2 levels indicated down-regulation, which was achieved after 5.8 days. In both groups the ovarian stimulation resulted in ovulatory cycles, while 4 pregnancies in group A and 1 in group B were achieved.

CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 14

IT **74381-53-6**, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of ovarian cysts following GnRH-a treatment in patients with polycystic ovarian syndrome)

IT **74381-53-6**, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of ovarian cysts following GnRH-a treatment in patients with polycystic ovarian syndrome)

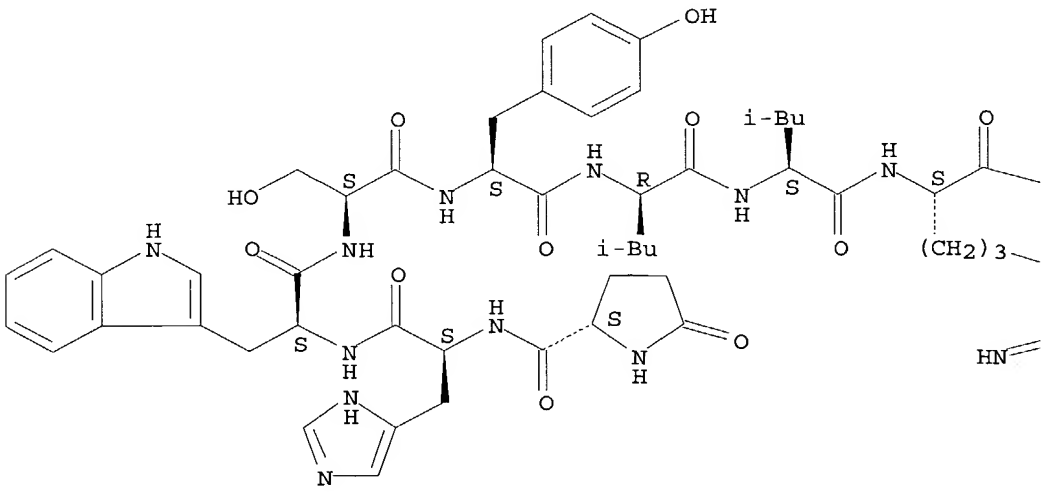
RN 74381-53-6 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

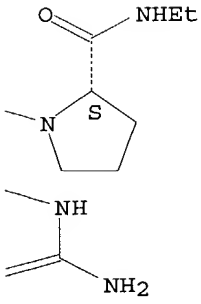
CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



CM 2

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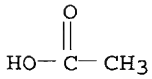


REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN

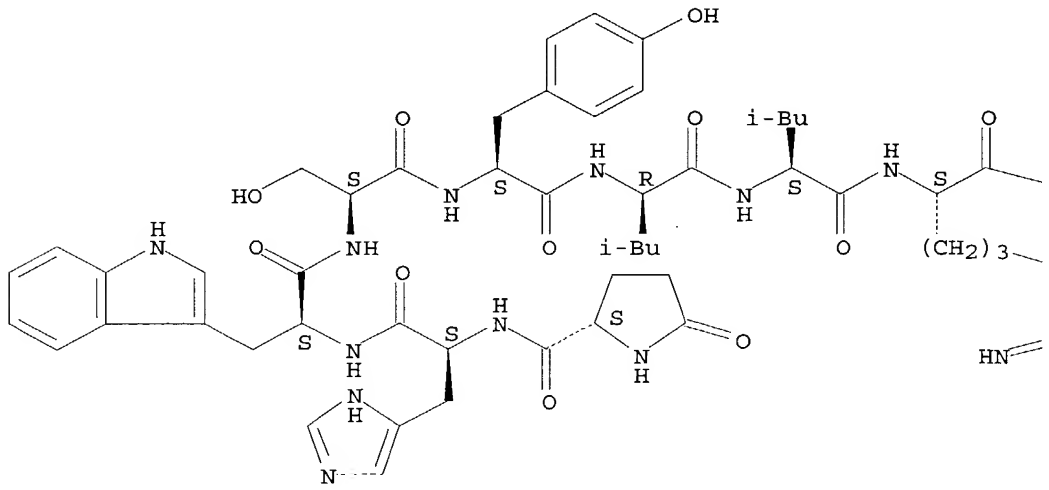
ACCESSION NUMBER: 1998:757320 CAPLUS
DOCUMENT NUMBER: 130:11012
TITLE: Management in Gynecology: The Role of a GnRH-a, Leuprorelin Acetate Depot. (Proceedings of a Symposium for the XVth FIGO World Congress of Gynecology and Obstetrics, Copenhagen, 6 August 1997.) [In: Gynecol. Obstet. Invest., 1998; 45(Suppl. 1)]
AUTHOR(S): Genazzani, Andrea R.; Editor
CORPORATE SOURCE: Switz.
SOURCE: (1998) Publisher: (Karger: Basel, Switz.), 35 pp.
DOCUMENT TYPE: Book
LANGUAGE: English
AB Unavailable
CC 2-5 (Mammalian Hormones)
IT **74381-53-6**, Leuprorelin acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH-analog leuprorelin acetate depot role gynecol.)
IT **74381-53-6**, Leuprorelin acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH-analog leuprorelin acetate depot role gynecol.)
RN 74381-53-6 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

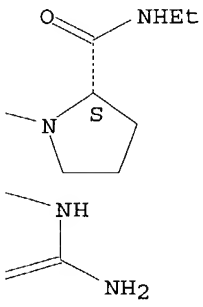
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

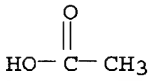
PAGE 1-A





CM 2

CRN 64-19-7
CMF C2 H4 O2



L13 ANSWER 9 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:743993 CAPLUS
DOCUMENT NUMBER: 130:134289
TITLE: Long-term neoadjuvant hormone therapy prior to radical prostatectomy: analysis of outcome by preoperative risk factors
AUTHOR(S): Gleave, Martin E.; Goldenberg, S. Larry; Jones, Edward C.; Bruchovsky, Nicholas; Sullivan, Lorne D.
CORPORATE SOURCE: Division of Urology, Vancouver General Hospital, University of British Columbia, Vancouver, BC, Can.
SOURCE: Molecular Urology (1998), 2(3), 171-177,179
CODEN: MOURFE; ISSN: 1091-5362
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A prospective Phase II trial was initiated to assess the effects of 8 mo of neoadjuvant hormone therapy on pathol. stage and biochem. recurrence rates. A total of 158 men with clin. localized prostate cancer were treated with neoadjuvant combined androgen withdrawal for 8 mo prior to radical prostatectomy. Preoperative clin. stage, Gleason score, and serum prostate specific antigen (PSA) were examined for influence on treatment outcome (pathol. stage and PSA recurrence). At diagnosis, PSA was <10 μg/L in 64%, 10 to 20 μg/L in 21%, and >20 μg/L in 15% (mean 11.5 μg/L). The clin. stage was T1c in 17%, T2a in 24%, T2b in 52%, and T3a in 7%. The gleason score was ≤4 in 31%, 5 or 6 in 47%, and ≥7 in 22%. The pathol. stage was T0 in 11%, T2 (organ confined) in 68%, T3 (specimen-confined) in 13%, T3 (margin pos.) in 5%, and TxN+ in 2%. High-risk factors (Stage T3a, Gleason ≥7, or PSA ≥10 μg/L) were present in 49% of patients. The risk of pos.-margin disease

increased with Stage T3a v organ-confined disease (25% v 4%), with pretreatment Gleason scores ≥7 v <7 (11% v 4%), and with pretreatment PSA ≥10 μg/L v <10 μg/L (15% v 0). The overall recurrence rate detected by PSA was 10% after a mean postoperative follow-up of 33 mo. The risk of PSA recurrence increased with clin. stage (18% T3 v 10% organ-confined), pretreatment PSA (5% when PSA was <10 μg/L v 17% when PSA was ≥10 μg/L), Gleason score (8% when ≤6 v 16% when ≥7), and pathol. stage (3% of pT2, 25% of pT3 margin neg. and 50% of pT3 margin pos.). Recurrences identified by PSA occurred in 5% of patients with no adverse preoperative risk factors, 16% of those with any one of the high-risk factors, and 23% of those with any two of the high-risk factors. Eight months of neoadjuvant therapy results in low pos.-margin rates and a low overall risk of biochem. recurrence. The risk of PSA recurrence remains proportional to the number of adverse preoperative risk factors. Randomized studies are required to determine whether a longer duration of neoadjuvant therapy will reduce the biochem. recurrence rate.

CC 2-4 (Mammalian Hormones)

IT 56-53-1, Diethylstilbestrol 427-51-0, Androcur 13311-84-7, Flutamide **74381-53-6**, Lupron
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long-term neoadjuvant hormone therapy prior to radical prostatectomy in humans with prostate cancer)

IT **74381-53-6**, Lupron
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long-term neoadjuvant hormone therapy prior to radical prostatectomy in humans with prostate cancer)

RN 74381-53-6 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

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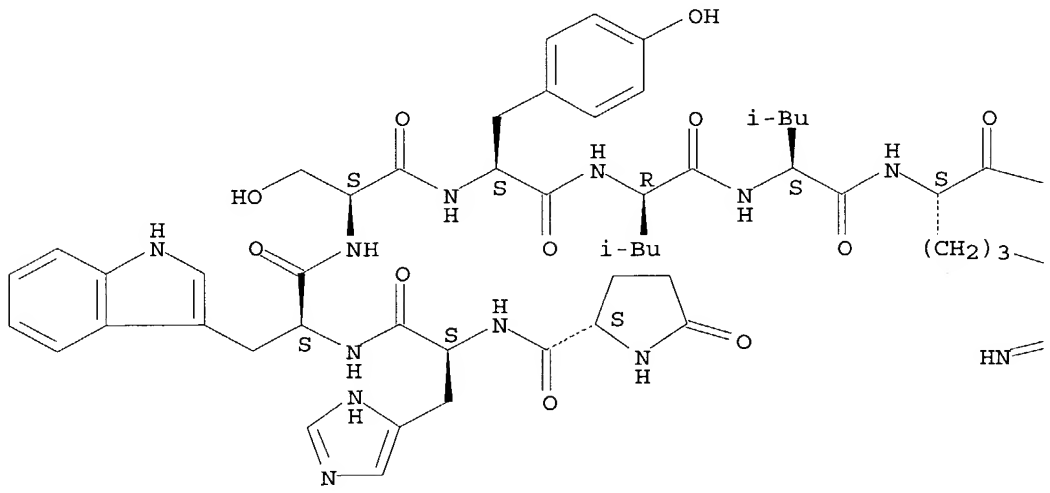

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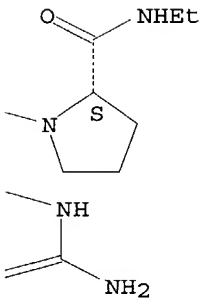

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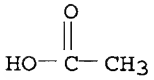


REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:743991 CAPLUS
DOCUMENT NUMBER: 130:134287
TITLE: Radical prostatectomy v radical prostatectomy preceded by combined androgen blockade in clinical stage B2 (T2bNxM0) prostate cancer: an update
AUTHOR(S): McLeod, David
CORPORATE SOURCE: Urology Service, Department of Surgery, Walter Reed Army Medical Center, Washington, DC, USA
SOURCE: Molecular Urology (1998), 2(3), 159-161,163-164
CODEN: MOURFE; ISSN: 1091-5362
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Between Feb. 1992 and Mar. 1994, the authors conducted a randomized multi-institutional trial in the United States. Patients received a radical prostatectomy or a radical prostatectomy preceded by 3 mo of androgen deprivation (3 mo of leuprolide acetate depot 7.5 mg with a fourth dose given 48 h prior to surgery and flutamide 250 mg orally every 8 h). There are 137 patients who had surgery following androgen depletion compared with 138 who had surgery alone who are evaluable for anal. to compare capsular penetration and surgical margins. Since the initial evaluation, there is now a 24-mo anal. of postoperative prostate specific antigen (PSA) data-129 patients with preoperative androgen deprivation and 127 who had surgery alone. Survival anal. was used to estimate relapse rates; i.e., PSA >0.4 ng/mL. The pretreated group had a lower rate of capsular penetration (47% v 78%) and were less likely to have pos. surgical margins (18% v 48%) and less at the urethral margin (6% v 17%). However, at this time (24 mo), there are 27 patients in both arms who have had recurrences, as judged by PSA. A pos. margin has been associated with a higher relapse rate in both groups. The authors' study shows fewer pos. margins and less capsular penetration in those patients pretreated with androgen deprivation. Although the PSA recurrence rates are the same for both groups at the present time, the authors feel that it is too soon to dismiss out-of-hand the use of neoadjuvant therapy.

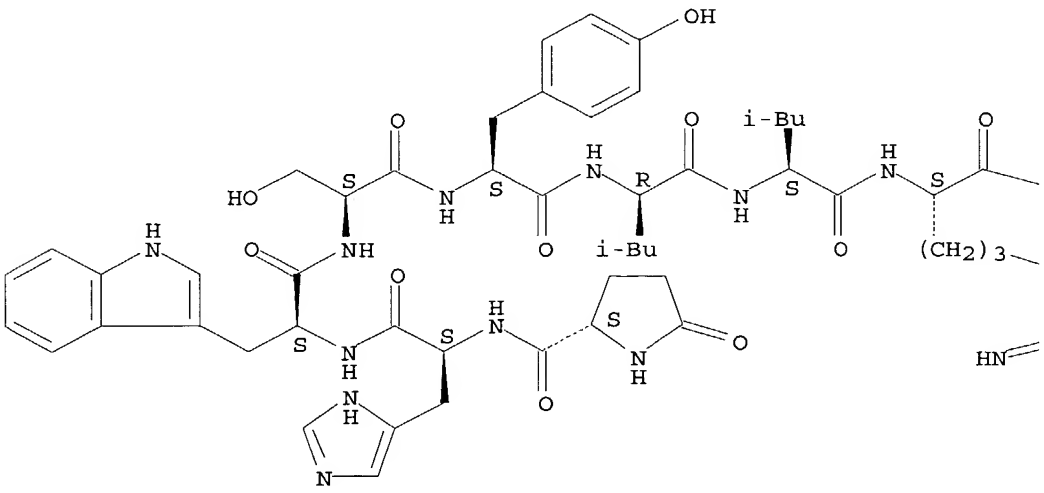
CC 2-4 (Mammalian Hormones)
IT 13311-84-7, Flutamide **74381-53-6**, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radical prostatectomy vs. radical prostatectomy preceded by combined androgen blockade in clin. stage B2 prostate cancer in humans)
IT **74381-53-6**, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radical prostatectomy vs. radical prostatectomy preceded by combined androgen blockade in clin. stage B2 prostate cancer in humans)
RN 74381-53-6 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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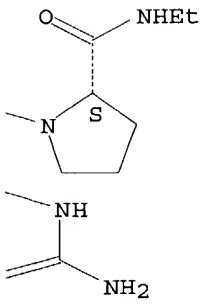

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CRN 64-19-7
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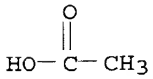

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:721273 CAPLUS
DOCUMENT NUMBER: 130:105436
TITLE: Prospective randomized study of the effect of "add-back" hormone replacement on vascular function during treatment with gonadotropin-releasing hormone agonists
AUTHOR(S): Yim, S. F.; Lau, T. K.; Sahota, D. S.; Chung, T. K. H.; Chang, A. M. Z.; Haines, C. J.
CORPORATE SOURCE: Department of Obstetrics and Gynaecology, Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, Peop. Rep. China
SOURCE: Circulation (1998), 98(16), 1631-1635
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objectives-Gonadotropin-releasing hormone agonists (GnRHas) are a group of drugs that with long-term use induce a pseudomenopausal state in which estrogen production is suppressed. They are commonly used in the treatment of sex steroid-dependent conditions. "Add-back" hormone replacement therapy is used to prevent menopause-like symptoms and bone loss during GnRHa treatment, but it is also recognized that hypoestrogenism adversely affects vascular function. The aim of this study was to examine the effect of GnRHa and add-back therapy on vascular reactivity. This model serves as a paradigm for the effect of hormone replacement therapy in postmenopausal women. Methods and Results-Measurements of endothelium-dependent and endothelium-independent vascular reactivity were compared in 2 groups of women treated with a GnRHa for 6 mo. One group received estrogen/progestogen add-back therapy during the second 3 mo of GnRHa treatment. Vascular reactivity was examined by use of ultrasound measurements of changes in brachial artery diameter Endothelium-dependent changes were assessed during reactive hyperemia, whereas endothelium-independent changes were measured after the administration of glyceryl trinitrate sublingual spray. Treatment with the GnRHa alone had an inhibitory effect on endothelium-dependent relaxation. However, endothelium-dependent relaxation significantly improved in the group receiving add-back therapy (14.6%) compared with the group treated with GnRHa alone (8.6%). There were no significant endothelium-independent changes in either group. Conclusions-These results suggest that the administration of add-back therapy has a protective effect on vascular function in GnRHa-induced hypoestrogenism. As a model for the menopause, these results also suggest that the long-term administration of hormone replacement therapy would result in endothelium-dependent arterial relaxation, an observation previously attributed only to the acute administration of estrogen.

CC 2-4 (Mammalian Hormones)

IT **74381-53-6**, Leuprorelin acetate
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(add-back hormone replacement on vascular function during treatment with gonadotropin-releasing hormone agonists in women)

IT **74381-53-6**, Leuprorelin acetate
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(add-back hormone replacement on vascular function during treatment with gonadotropin-releasing hormone agonists in women)

RN 74381-53-6 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

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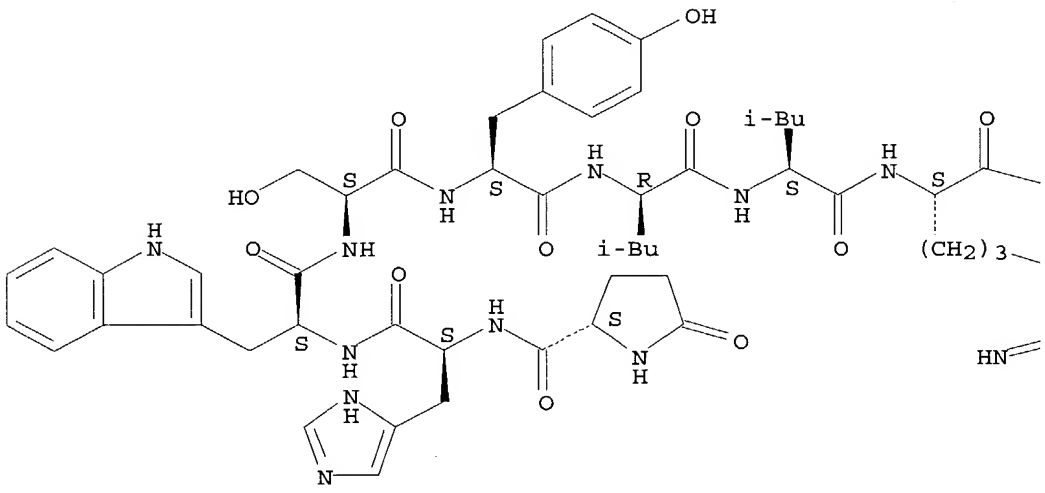
CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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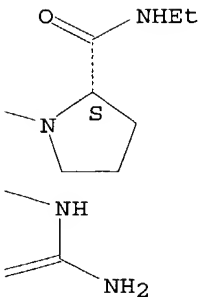

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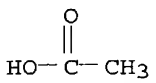


REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:702924 CAPLUS
DOCUMENT NUMBER: 130:76325
TITLE: Supersensitive PSA-monitored neoadjuvant hormone treatment of clinically localized prostate cancer: effects on positive margins, tumor detection and epithelial cells in bone marrow
AUTHOR(S): Kollermann, M. W.; Pantel, K.; Enzmann, Th.; Feek, U.; Kollermann, J.; Kossiwakis, M.; Kaulfuss, U.; Martell, W.; Spitz, J.
CORPORATE SOURCE: Department of Urology, Dr. Horst Schmidt Kliniken, Wiesbaden, D-65199, Germany
SOURCE: European Urology (1998), 34(4), 318-324
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study was done to investigate the effects of supersensitive PSA-controlled inductive treatment on pos. margins, detection of tumor and epithelial cells in bone marrow of 101 patients with untreated and clin. localized prostatic carcinoma (cT1-3N0M0). Hormonal treatment was given until PSA (DPD Immulite third-generation assay) reached <0.1 ng/mL or the nadir value, as shown by two consecutive measurements at monthly intervals. The resultant median duration of treatment was 6 mo (range 3-22). Ninety-three (93%) of the patients reached a PSA value <0.1 ng/mL. The nadir of 6 patients (6%) was between 0.1 and 0.3 ng/mL, and it remained >0.3 ng/mL in only 1 case. Of the 101 patients, 82 had a measurable hypoic lesion on initial transrectal ultrasound. Of these, 84% became smaller, 7.5% remained unchanged and 8.5% increased. Of the 101 prostatectomy specimens, 20 (20%) were margin-pos. The incidence of affected margins was relatively high (35% from 55 patients) with cT3 tumors but almost negligible (2% from 46 patients) in cT1-2 tumor. The pathologists despite their great experience in evaluating hormonally treated prostate (>500 cases) and using immunohistochem. staining, were unable to detect carcinoma in 15 (15%) specimens. Whereas only 2 (4%) of the 55 cT3 specimens were without detectable tumor, this incidence rose to 28% (13 of 46 prostates) in patients with cT1-2 tumors. Of the initial 29 patients with epithelial cells in bone marrow, only 4 (14%) remained pos. after controlled induction and all of them had fewer cells than before. Endocrine induction controlled by a supersensitive PSA assay and continued until reaching PSA nadir is highly effective in clearing surgical margins and eliminating tumor cells from bone marrow. It seems to be clearly superior to the conventional 3 mo of pretreatment at least in cT1-2 tumors in respect to surgical margins and detectability of tumor in the resected prostate. A definitive statement about the value of endocrine induction can only be given by prospective randomized studies, with optimal drugs, doses and treatment time. But the conventional 3 mo of pretreatment are far from exploiting the possibilities of this therapeutic option.

CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 14
IT 9034-40-6D, LH-RH, agonist analogs **74381-53-6**, Leuprorelin

acetate 196966-24-2, Fugerel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoadjuvant hormone treatment effects on PSA, pos. margins, tumor detection and epithelial cells in bone marrow in localized prostate cancer in men)

IT **74381-53-6**, Leuprorelin acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoadjuvant hormone treatment effects on PSA, pos. margins, tumor detection and epithelial cells in bone marrow in localized prostate cancer in men)

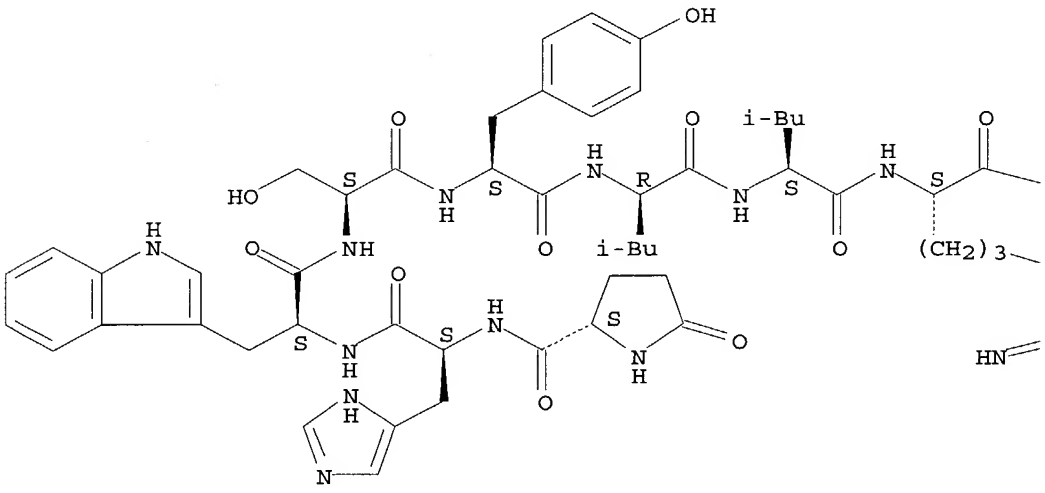
RN 74381-53-6 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

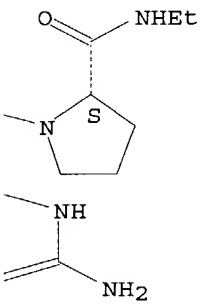
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A





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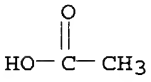

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L13 ANSWER 13 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:697235 CAPLUS
DOCUMENT NUMBER: 129:286174
TITLE: Effects of Ringer's lactate, medroxyprogesterone acetate, gonadotropin-releasing hormone analog and its diluent on the prevention of postsurgical adhesion formation in rat models
AUTHOR(S): Ustun, C.; Yanik, Filiz F.; Kocak, I.; Canbaz, M. A.; Cayli, R.
CORPORATE SOURCE: Dep. Obstetrics Gynecology, School Medicine, Ondokuz Mayis Univ., Samsun, 55060, Turk.
SOURCE: Gynecologic and Obstetric Investigation (1998), 46(3), 202-205
CODEN: GOBIDS; ISSN: 0378-7346
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The efficacy of medroxyprogesterone acetate (MPA), leuprolide acetate (LA), and Ringer's lactate was examined in the prevention of postoperative adhesion formation in rats. Before the standard surgical procedure, which consisted of creating a lesion with electrocautery over the uterus, LA was injected together with its diluent, the diluent of LA alone, and MPA. Ringer's lactate solution was applied i.p. at the end of the surgery. After 3 wk, the postsurgical adhesions were less in the groups treated with Ringer's lactate, LA, and MPA.
CC 2-4 (Mammalian Hormones)

IT 71-58-9, Medroxyprogesterone acetate **74381-53-6**, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prevention of postsurgical adhesions)

IT **74381-53-6**, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prevention of postsurgical adhesions)

RN 74381-53-6 CAPLUS

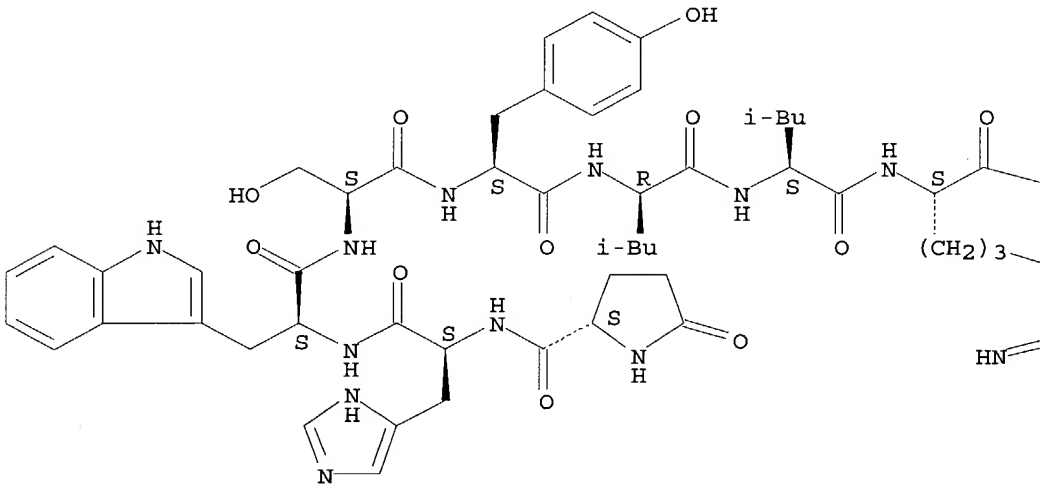
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

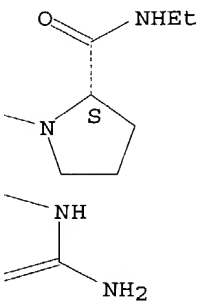
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A





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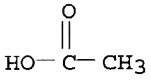


L13 ANSWER 14 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:630123 CAPLUS
DOCUMENT NUMBER: 129:340026
TITLE: Regulation of follicular luteinization by a gonadotropin-releasing hormone agonist: relationship between steroidogenesis and apoptosis
AUTHOR(S): Andreu, Claudia; Parborell, Fernanda; Vanzulli, Silvia; Chemes, Hector; Tesone, Marta
CORPORATE SOURCE: Instituto de Biologia y Medicina Experimental, CONICET, Buenos Aires, Argent.
SOURCE: Molecular Reproduction and Development (1998), 51(3), 287-294
CODEN: MREDEE; ISSN: 1040-452X
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to evaluate the effects of GnRH-analog (Leuprolide acetate, LA) administration on follicular luteinization in equine chorionic gonadotropin plus human chorionic gonadotropin (eCG + hCG)-superovulated prepubertal treated rats. Results indicate that LA treatment decreases circulating levels of progesterone (P) and P accumulation in collagenase-dispersed ovarian cell cultures, though estradiol (E2) production is increased. These data suggest that cells from the LA group may be less luteinized following gonadotropin treatment. Studies performed on histol. ovarian sections after different times of eCG administration showed that LA injections produce lower amts. of corpora lutea and antral follicles, and a greater number of atretic and preantral follicles. The basal and LH-stimulated P and progestogen accumulations

are decreased in incubations of corpora lutea isolated from the LA group. In addition, the mitochondrial cholesterol side-chain cleavage (P 450SCC) levels in corpora lutea from LA-treated rats are reduced, indicating that the decrease in P production observed is due in part to an alteration in the steroidogenic luteal capability. Immunocytochem. localization of nuclei exhibiting DNA fragmentation by the technique of terminal deoxynucleotidyl transferase end-labeling showed that LA treatment causes an increase in the number of apoptotic cells in preantral and antral follicles at all times studied (1, 2, 4, or 7 days of LA administration). A similar effect, though less pronounced, was observed in corpora lutea. It is concluded that LA treatment produces a failure in the steroidogenic luteal capability and an increase of apoptotic mechanisms in the ovary, producing as a consequence an interference in the follicular recruitment, growth, and luteinization induced by gonadotropins.

CC 2-5 (Mammalian Hormones)

IT 9002-61-3, Chorionic gonadotropin 9002-67-9, LH 9002-70-4, Pregnant mare serum gonadotropin **74381-53-6**, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(LH-RH agonist regulation of follicular luteinization and relationship between steroidogenesis and apoptosis)

IT **74381-53-6**, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(LH-RH agonist regulation of follicular luteinization and relationship between steroidogenesis and apoptosis)

RN 74381-53-6 CAPLUS

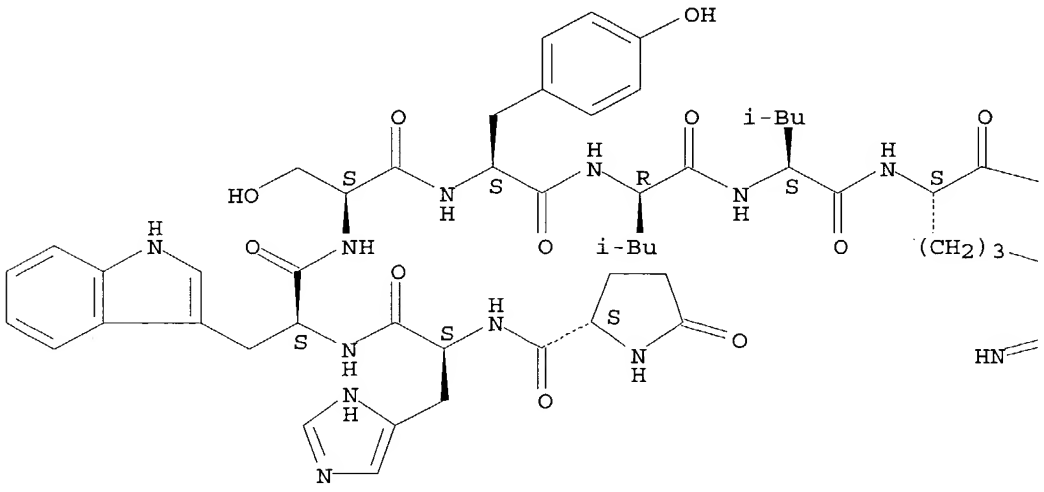
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

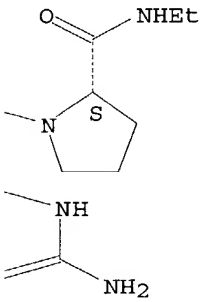
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

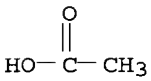
PAGE 1-A





CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 15 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:550205 CAPLUS
DOCUMENT NUMBER: 129:286143
TITLE: Stronger suppression of serum testosterone and FSH levels by a synthetic estrogen than by castration or an LH-RH agonist
AUTHOR(S): Kitahara, Satoshi; Yoshida, Ken-ichiro; Ishizaka, Kazuhiro; Kageyama, Yukio; Kawakami, Satoru; Tsujii, Toshihiko; Oshima, Hiroyuki
CORPORATE SOURCE: Department of Urology, Tokyo Medical and Dental University School of Medicine, Tokyo, 113, Japan
SOURCE: Endocrine Journal (Tokyo) (1997), 44(4), 527-532
CODEN: ENJOEO; ISSN: 0918-8959
PUBLISHER: Japan Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Serum levels of LH, FSH and testosterone (T) were measured by RIAs in 36 patients with advanced prostate cancer before and during androgen ablation therapies. Both leuprolide acetate (LH-RH agonist: LHRH-A) and diethylstilbestrol diphosphate (DES-DP) administration decreased serum LH significantly to an undetectable level (LHRH-A:, DES-DP:). LHRH-A and DES-DP diminished serum FSH to 20% of the pre-treatment level and to an undetectable level, resp. LHRH-A and DES-DP decreased serum T to the castration level and an undetectable level, resp. Serum levels of the same 3 hormones before and after DES-DP administration were measured in 8

patients who received DES-DP after LHRH-A treatment or castration because of relapse of the disease. DES-DP lowered serum FSH further than LHRH-A to an undetectable level and diminished T further than previous treatments to an undetectable level (vs. LHRH-A, vs. castration). These results suggest that (1) DES-DP is able to reduce T production from extra-testicular site(s), and achieve the minimal serum T level, and this DES-DP action appears to be one of the mechanisms of the effectiveness of estrogen on refractory prostate cancer after castration or LHRH-A. In addition, basal (independent of LH-RH) FSH secretion in elderly men is about 20% of total FSH secretion and DES-DP inhibits the basal FSH secretion at the level of the pituitary.

CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 1

IT 522-40-7, Diethylstilbestrol diphosphate **74381-53-6**, Leuprolide acetate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stronger suppression of serum testosterone and FSH levels by a synthetic estrogen than by castration or an LH-RH agonist)

IT **74381-53-6**, Leuprolide acetate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stronger suppression of serum testosterone and FSH levels by a synthetic estrogen than by castration or an LH-RH agonist)

RN 74381-53-6 CAPLUS

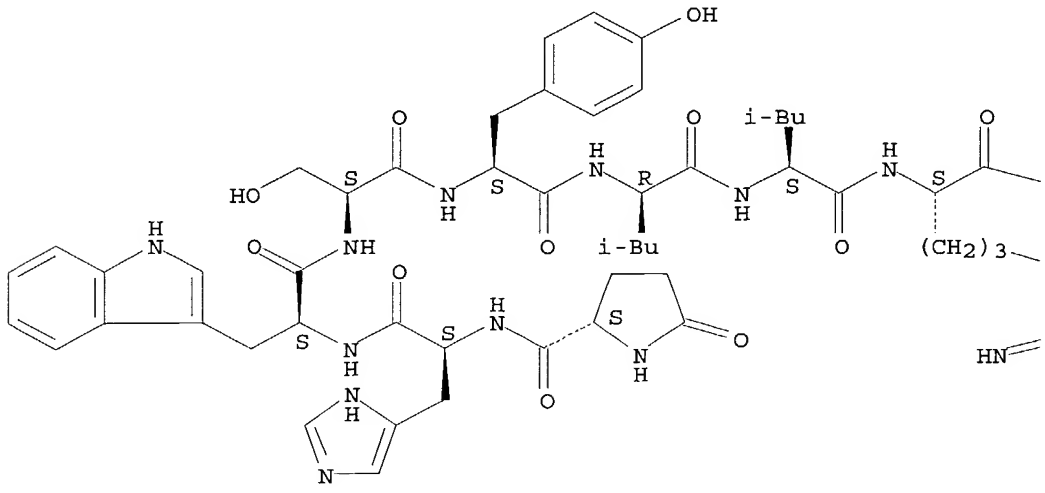
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

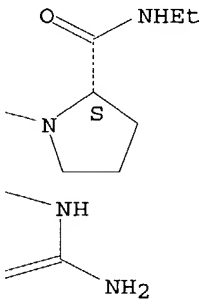
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A





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CRN 64-19-7
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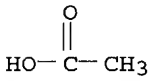


REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 16 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:550200 CAPLUS
DOCUMENT NUMBER: 129:286189
TITLE: Clinical usefulness of urinary CrossLaps as a sensitive marker of bone metabolism
AUTHOR(S): Nakayama, Hirotoshi; Yano, Tetsu; Sagara, Yoko; Ando, Kayo; Kasai, Yasuyo; Taketani, Yuji
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Faculty of Medicine, University of Tokyo, Tokyo, 113, Japan
SOURCE: Endocrine Journal (Tokyo) (1997), 44(4), 479-484
CODEN: ENJOEO; ISSN: 0918-8959
PUBLISHER: Japan Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CrossLaps peptide [Glu-Lys-Ala-His-Asp-Gly-Gly-Arg], a part of the C-telopeptide of the α1-chain of type I collagen of bone, is a recently developed biochem. marker of bone turnover. In this study, the clin. utility of measurement of urinary CrossLaps was investigated in eleven premenopausal women who received a gonadotropin-releasing hormone (GnRH) agonist for 6 mo for treatment of adenomyosis or leiomyomas. Along with urinary CrossLaps, the levels of various biochem. markers, and serum estradiol, calcitonin and intact parathyroid hormone (i-PTH) were measured, and lumbar spine bone mineral d. (BMD) was also monitored before, during, and at the end of the course of GnRH agonist therapy. Apart from CrossLaps, markers of bone resorption tested were urinary pyridinoline, deoxypyridinoline and hydroxyproline. Markers of bone

formation tested were serum osteocalcin and bone-specific alkaline phosphatase (B-ALP). Serum estradiol levels decreased to undetectable levels at 2 mo of GnRH agonist therapy. The values for all biochem. markers increased significantly throughout the therapy. The degree of an increase in CrossLaps levels was greater than that in all other markers. Mean lumbar spine (L2-L4) BMD was decreased by 7.2% at 6 mo of treatment. The percent change in BMD at 6 mo of treatment correlated inversely with the percent change in CrossLaps levels from the baseline to 1, 2, and 5 mo of treatment. These results indicate that measurement of urinary CrossLaps might be a useful tool to predict the risk of bone loss caused by hypoestrogenism including GnRH agonist therapy.

CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 9

IT **74381-53-6**, Leuplin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urinary CrossLaps as marker of bone metabolism in premenopausal women treated with LH-RH agonist)

IT **74381-53-6**, Leuplin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urinary CrossLaps as marker of bone metabolism in premenopausal women treated with LH-RH agonist)

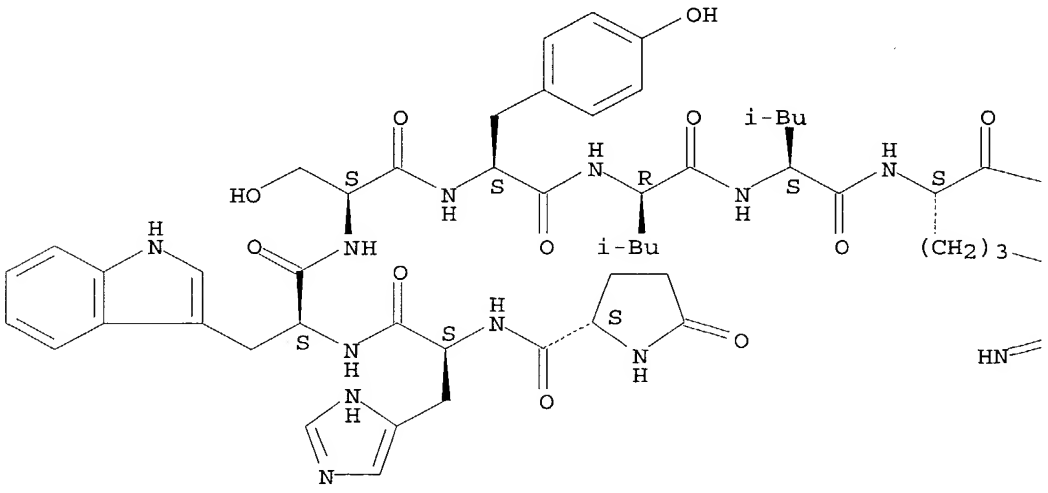
RN 74381-53-6 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

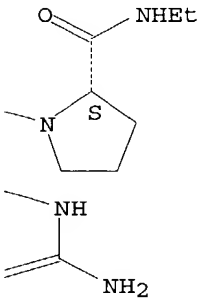
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A





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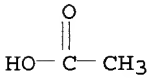
CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 17 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:550198 CAPLUS
DOCUMENT NUMBER: 129:286188
TITLE: Restoration of seminiferous tubular function after discontinuation of long-term gonadotropin-releasing hormone agonist administration in premature male rats
AUTHOR(S): Ohyama, Kenji; Ohta, Masanori; Nakagomi, Yoshiko; Shimura, Yoshie; Sano, Tomoaki; Sato, Kazumasa; Nakazawa, Shinpei; Ishikawa, Hiromichi
CORPORATE SOURCE: Department of Pediatrics, Yamanashi Medical University, Yamanashi, 409-38, Japan
SOURCE: Endocrine Journal (Tokyo) (1997), 44(4), 459-465
CODEN: ENJOEO; ISSN: 0918-8959
PUBLISHER: Japan Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We examined whether seminiferous tubular function develops normally after discontinuation of long-term gonadal suppression in premature male rats. Wistar male rats 4 wk old were subjected to the injection of gonadotropin-releasing hormone (Gn-RH) agonist or normal saline solution as control for 12 wk. The rats were sacrificed 0 and 6 wk after discontinuation of the treatment. Histol. examns. of the seminiferous tubules immediately after cessation of the Gn-RH agonist treatment demonstrated a stage-related change in specific germ cells. Seminiferous tubules of Gn-RH agonist-treated rats were narrow and irregular in shape, and contained significantly fewer spermatids and pachytene spermatocytes

at stages VII to XIV than those in controls. A complete development of spermatogenesis was histol. observed 6 wk after cessation of the treatment. Leydig cells became atrophic without any reduction in cell number immediately after the treatment, but Leydig cells grew rapidly and were similar in appearance to those in control rats 6 wk after cessation of the treatment. Serum testosterone concns. were noticeably suppressed immediately after cessation of the treatment and reached a similar level to those of controls 6 wk after the cessation. Testes wts. were significantly lower in Gn-RH agonist-treated rats than in control rats and had not fully developed 6 wk after cessation of the treatment. These results suggest that the testicular function develops normally after cessation of the long-term gonadal suppression in premature rats, although the increase in testicular weight may be slightly influenced.

CC 2-5 (Mammalian Hormones)

IT **74381-53-6**, Leuprorelin acetate
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(seminiferous tubular function restoration after long-term LH-RH agonist discontinuation in premature male rats)

IT **74381-53-6**, Leuprorelin acetate
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(seminiferous tubular function restoration after long-term LH-RH agonist discontinuation in premature male rats)

RN 74381-53-6 CAPLUS

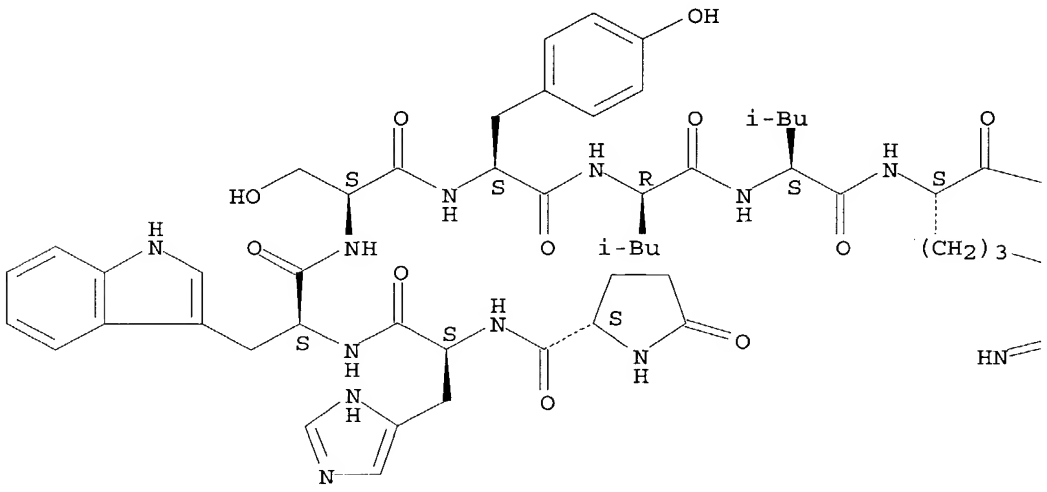
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

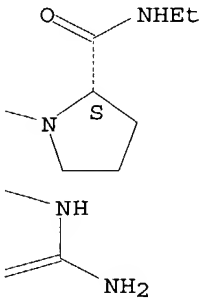
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A





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CRN 64-19-7
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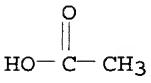


REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 18 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:547337 CAPLUS
DOCUMENT NUMBER: 129:255265
TITLE: GnRH analogs and steroids in the enhancement of recovery of spermatogenesis from cytotoxic treatment
AUTHOR(S): Meistrich, M.; Wilson, G.; Kurdoglu, B.
CORPORATE SOURCE: Dep. Experimental Radiation Oncology, Univ. Texas M. D. Anderson Cancer Cent., Houston, TX, USA
SOURCE: Current Advances in Andrology, Proceedings of the International Congress of Andrology, 6th, Salzburg, May 25-29, 1997 (1997), 355-361. Editor(s): Waites, Geoffrey M. H.; Frick, Julian; Baker, Gordon W. H. Monduzzi Editore: Bologna, Italy.
CODEN: 66MSAS
DOCUMENT TYPE: Conference
LANGUAGE: English
AB After irradiation or other cytotoxic injury to the rat testis, there is an initial phase of recovery of spermatogenesis from surviving stem cells, but then the percentage of tubules showing active spermatogenesis progressively declines despite the presence of proliferating A spermatogonia in these tubules. Treatment of the rats immediately after irradiation with steroid hormones or GnRH agonist prevents this decline in the percentage of tubules showing active spermatogenesis. The recovery of spermatogenesis can also be stimulated even if initiation of the GnRH-agonist treatment is delayed for several months until after the

decline in spermatogenesis has occurred. Even after the cessation the hormone treatment, the further recovery of spermatogenesis continues to progress. The mechanism by which recovery is stimulated is not yet known; since both steroid and hormone treatments and GnRH agonists lower intratesticular levels of testosterone, the authors suggest that the high intratesticular testosterone levels observed after irradiation may be indirectly
inhibitory to spermatogonial differentiation, and lowering of these levels is required to stimulate recovery.

CC 2-5 (Mammalian Hormones)

IT **74381-53-6**, Lupron
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH analogs and steroids enhance recovery of spermatogenesis from cytotoxic treatment)

IT **74381-53-6**, Lupron
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH analogs and steroids enhance recovery of spermatogenesis from cytotoxic treatment)

RN 74381-53-6 CAPLUS

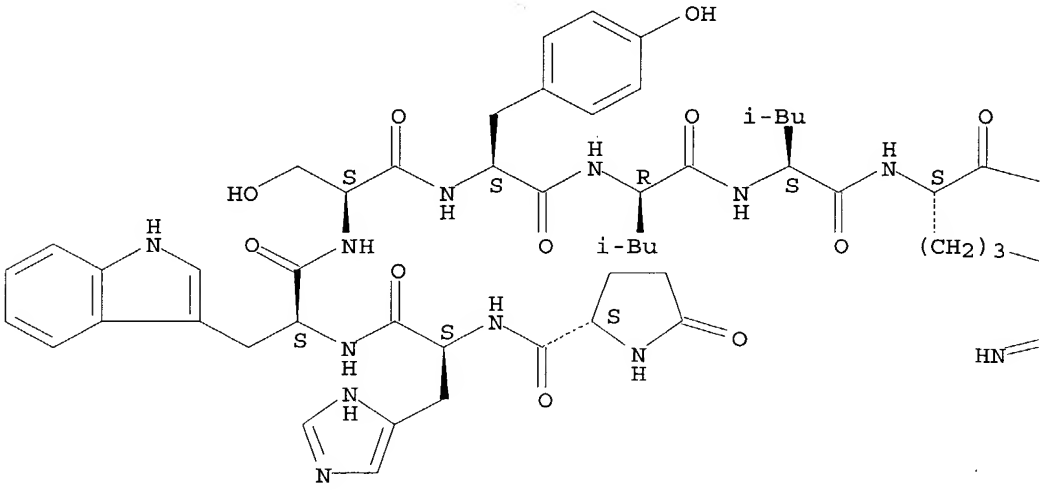
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

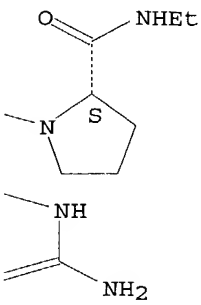
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A





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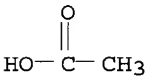


REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 19 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:539377 CAPLUS
DOCUMENT NUMBER: 129:286182
TITLE: Timing for discontinuation of treatment with a long-acting gonadotropin-releasing hormone analog in girls with central precocious puberty
AUTHOR(S): Ohyama, Kenji; Tanaka, Toshiaki; Tachibana, Katsuhiko; Niimi, Hiroo; Fujieda, Kenji; Matsuo, Nobutake; Satoh, Mari; Hibi, Itsuro
CORPORATE SOURCE: Members of the TAP-144SR CPP Study Group, Department of Pediatrics, Yamanashi Medical University, Yamanashi, 409-3898, Japan
SOURCE: Endocrine Journal (Tokyo) (1998), 45(3), 351-356
CODEN: ENJOEO; ISSN: 0918-8959
PUBLISHER: Japan Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The optimal timing for discontinuing treatment with a long-acting gonadotropin-releasing hormone (GnRH) analog (TAP-144SR) was investigated in patients with central precocious puberty (CPP). Thirty-five girls with CPP (21 with idiopathic disease and 14 with organic disease) were treated with the analog for 3 to 5 yr. No significant differences were seen between the idiopathic and the organic CPP in the suppressive effect of bone maturation. Advancement of bone maturation was noticeably suppressed during the period between bone ages (BA) of 11.0 and 11.9. The height standard deviation score (Ht-SDS) for BA was consistently improved from 10 to

11.5 yr of BA, and patients reached peak Ht-SDS at a BA of 11.5 yr. The ΔHt-SDS (annual change in Ht-SDS) was noticeably decreased at BA over 12 yr in spite of prolongation of the treatment. In the eight patients who have reached final height, the average Ht-SDS was -0.49 at end of the treatment (BA 11.7 yr) and the final Ht-SDS was -1.1 SD, resp. Predicted adult height at the end of the treatment was significantly higher than the actual final height ($P<0.01$). The results suggest that a fall in Ht-SDS for BA which usually occurs at approx. 12 yr of BA, is an indication for cessation of the treatment with TAP-144SR, and residual growth potential judged solely from BA may be decreased in girls with CPP after discontinuation of the treatment.

CC 2-5 (Mammalian Hormones)

IT **74381-53-6**, TAP 144SR
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long-acting gonadotropin-releasing hormone analog discontinuation timing in girls with central precocious puberty)

IT **74381-53-6**, TAP 144SR
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long-acting gonadotropin-releasing hormone analog discontinuation timing in girls with central precocious puberty)

RN 74381-53-6 CAPLUS

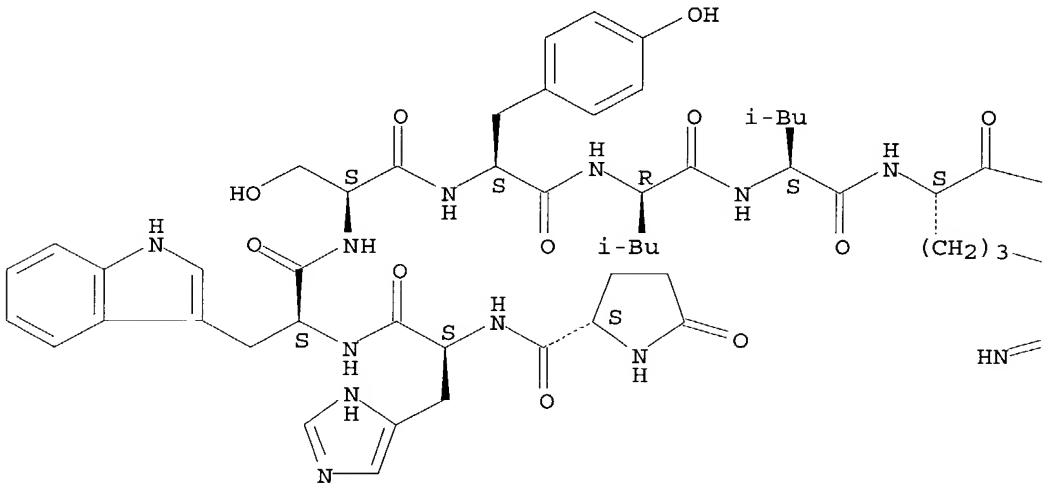
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

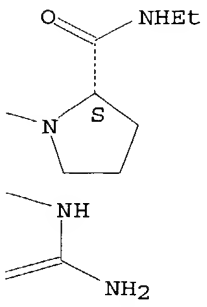
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A





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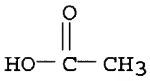


REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 20 OF 226 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:514864 CAPLUS
DOCUMENT NUMBER: 129:255182
TITLE: Effects of short-term suppression of ovarian hormones on cardiovascular and neuroendocrine reactivity to stress in women
AUTHOR(S): Matthews, Karen A.; Berga, Sarah L.; Owens, Jane F.; Flory, Janine D.
CORPORATE SOURCE: Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA, 15213, USA
SOURCE: Psychoneuroendocrinology (1998), 23(4), 307-322
CODEN: PSYCDE; ISSN: 0306-4530
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study reduced the levels of ovarian hormones to early postmenopausal levels by a GnRH agonist and evaluated the effects of a temporary suppression of ovarian hormones on premenopausal women's cardiovascular and neuroendocrine responses to laboratory challenges. The stress responses of 24 healthy young women were evaluated during three tasks during the early follicular phase and then after three monthly injections of Lupron, which suppressed their levels of estradiol, FSH, and LH. Thereafter, half the group resumed menstrual cycles (labeled Cycle), and half continued having Lupron injections in combination with transdermal estradiol (labeled Patch) and all were reevaluated a third time. A third group (labeled Control) of 12 women had four monthly injections of Lupron first and then were evaluated the first time. After

their cycles resumed, they were reevaluated twice 3 mo apart. Results showed that the magnitude of the blood pressure and catecholamine changes declined over the three evaluations, suggesting that the women's stress responses habituated. Although the suppression of ovarian hormone levels led to alterations in ovarian hormones for several months, which were accompanied by typical menopausal symptoms, cardiovascular and neuroendocrine responses to stress did not vary. This study did not test the effects of current estrogen exposure or of long term suppression of ovarian hormones upon cardiovascular and neuroendocrine responses.

CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 14

IT **74381-53-6**, Lupron
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(ovarian hormone short-term suppression effect on cardiovascular and neuroendocrine reactivity to stress in women)

IT **74381-53-6**, Lupron
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(ovarian hormone short-term suppression effect on cardiovascular and neuroendocrine reactivity to stress in women)

RN 74381-53-6 CAPLUS

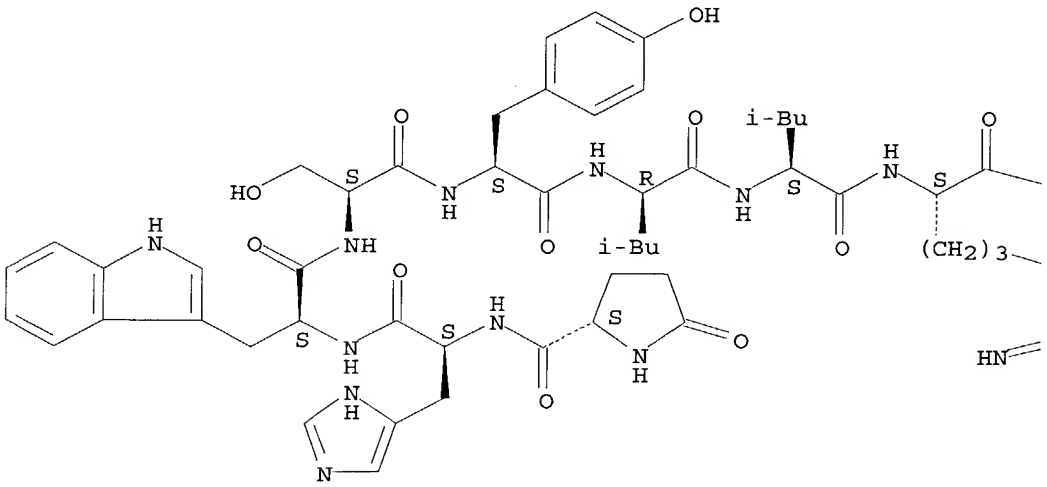
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monoacetate (salt) (9CI) (CA INDEX NAME)

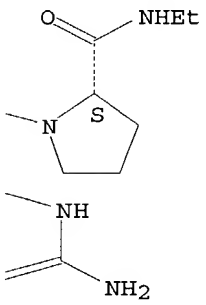
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

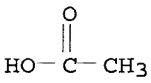
PAGE 1-A





CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 1 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:712316 CAPLUS
DOCUMENT NUMBER: 132:293988
TITLE: A facile method for synthesis of peptide alkylamide by solid phase method using Merrifield resin and Fmoc strategy
AUTHOR(S): Ohnuma, Saika; Sasaki, Yusuke
CORPORATE SOURCE: Tohoku Coll. Pharm., Sendai, 981-8558, Japan
SOURCE: Annual Report of the Tohoku College of Pharmacy (1998), 45, 175-183
CODEN: TYKNAQ; ISSN: 0495-7342
PUBLISHER: Tohoku Yakka Daigaku
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB A facile method for the synthesis of C-terminal peptide alkylamides was reported. The method involves the combined use of solid phase peptide synthesis on the Merrifield resin by Fmoc/tBu strategy, and aminolysis reaction of the resulting peptide resin with corresponding alkylamines in dichloromethane. The aminolysis reaction generally proceeded smoothly within 20 h by treatment with 6 M alkylamines. This facile method was successfully applied to the synthesis of Leuprolide (pGlu-His-Trp-Ser-Tyr-D-Leu-Leu-Arg-Pro-NH-Et).
CC 34-3 (Amino Acids, Peptides, and Proteins)

IT 74-89-5, Methylamine, reactions 75-04-7, Ethylamine, reactions 78-81-9, Isobutylamine 147-85-3D, L-Proline, Merrifield resin-bound, reactions 35661-60-0 **53714-56-0**, Leuprolide 86061-00-9 126855-21-8D, H-Tyr-Val-Phe-OH, Merrifield resin-bound 249927-01-3D, H-Tyr-Arg-Leu-OH, Merrifield resin-bound 264258-18-6D, H-Tyr-Asp-Gly-Phe-OH, Merrifield resin-bound 264258-19-7D, Merrifield resin-bound
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of peptide alkylamide by aminolysis of Merrifield resin-supported peptides with alkylamines)

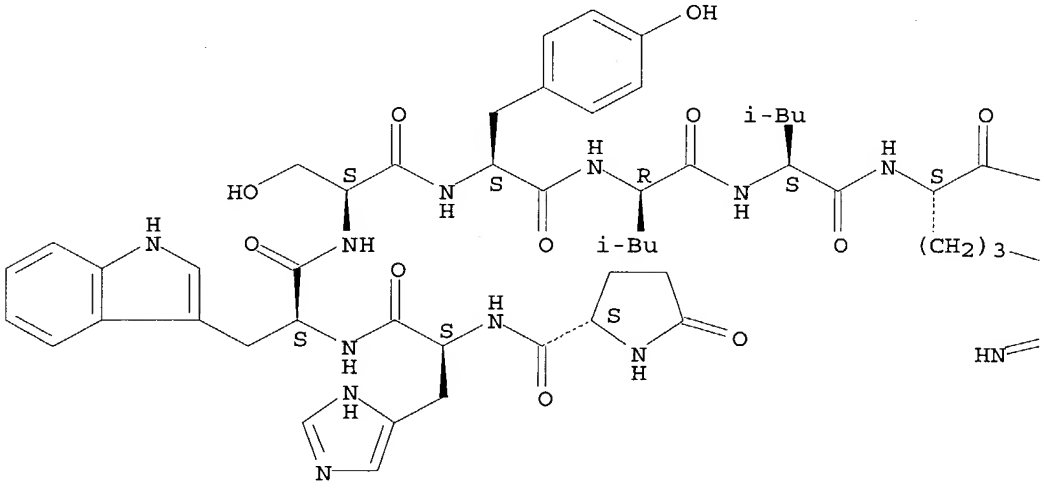
IT **53714-56-0**, Leuprolide
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of peptide alkylamide by aminolysis of Merrifield resin-supported peptides with alkylamines)

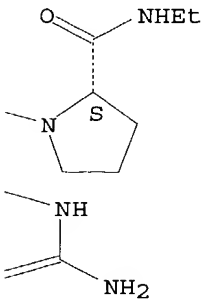
RN 53714-56-0 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A





L14 ANSWER 2 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:60760 CAPLUS
DOCUMENT NUMBER: 130:262376
TITLE: Differential inhibitory effects on human endometrial carcinoma cell growth of luteinizing hormone-releasing hormone analogs
AUTHOR(S): Borri, Patrizia; Coronnello, Marcella; Noci, Ivo; Pesciullesi, Alessandra; Peri, Alessandro; Caligiani, Raffaella; Maggi, Mario; Torricelli, Francesca; Scarselli, Gianfranco; Chieffi, Orlando; Mazzei, Teresita; Mini, Enrico
CORPORATE SOURCE: Istituto di Clinica Ginecologica ed Ostetrica, Universita degli Studi di Firenze, Florence, 50134, Italy
SOURCE: Gynecologic Oncology (1998), 71(3), 396-403
CODEN: GYNOA3; ISSN: 0090-8258
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In addition to its function as a key hormone in the regulation of the pituitary-gonadal axis, LH-releasing hormone (LHRH) probably also affects various extrapituitary tissues. LHRH binding sites and in vitro antiproliferative effects of LHRH analogs have been reported in human endometrial cancer. The effects of the LHRH agonist leuprorelin and LHRH antagonist antide were studied on the cell growth, DNA synthesis, and cell cycle distribution of the human endometrial cancer cell lines HEC-1A and HEC-1B by the sulforhodamine B (SRB) method, [3H]thymidine assay incorporation, and propidium iodide DNA staining, resp. In the presence of 1.0-100 μM leuprorelin the proliferation of HEC-1A cells was significantly reduced as early as 3 days after drug exposure, with a min. growth value of 69.9±3.6% (mean ± SE) at the highest concentration tested (100 μM). Similar antiproliferative effects were obtained following a 6-day treatment with the LHRH antagonist antide. Also, inhibitory effects on [3H]thymidine incorporation into the DNA of the HEC-1A cell line were noted after a 6-day exposure to both LHRH analogs, in the above-mentioned concentration range. Cell cycle anal. of HEC-1A cells cultured in the presence of 10 μM leuproreline and antide showed a slight accumulation of cells in the G0/G1 phase, while the proportions of cells in the S and G2/M phases concomitantly decreased. No significant effects on proliferation, DNA synthesis, and cell cycle distribution were observed in HEC-1B cells with

either leuprorelin or antide (up to 100 and 10 μM, resp.) after a 6-day exposure. Both Northern blot anal. and reverse transcription polymerase chain reaction failed to detect expression of mRNA for the LHRH receptor in both HEC-1A and HEC-1B cell lines. In addition, the LHRH analogs did not affect the intracellular free calcium concentration, indicating that the classic signal transduction for LHRH is absent or impaired in HEC-1A cells. The observed direct inhibitory actions on HEC-1A cells support the concept that the two LHRH analogs may exert biol. effects via cellular effectors distinct from the "classic" LHRH receptor. Although the mechanism by which these direct actions are produced is still obscure, these results might help to establish the basis for new approaches to the therapy of endometrial cancer. (c) 1998 Academic Press.

CC 2-5 (Mammalian Hormones)

IT **53714-56-0**, Leuprorelin 112568-12-4, Antide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of LHRH analogs on cell growth, DNA synthesis, and cell cycle distribution in two human endometrial cancer cell lines in relation to the expression of functional LHRH receptor)

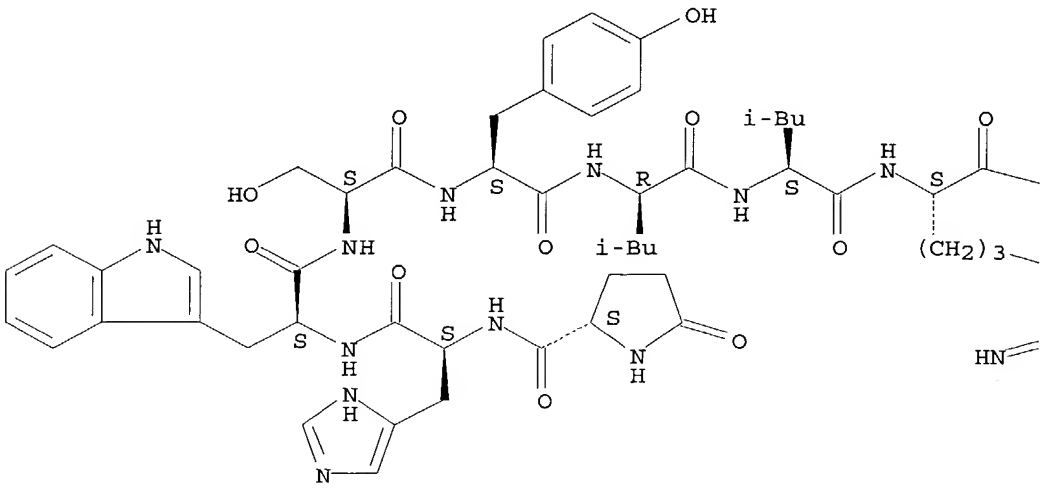
IT **53714-56-0**, Leuprorelin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of LHRH analogs on cell growth, DNA synthesis, and cell cycle distribution in two human endometrial cancer cell lines in relation to the expression of functional LHRH receptor)

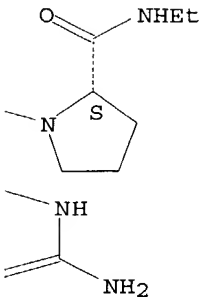
RN 53714-56-0 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A





REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:23744 CAPLUS
DOCUMENT NUMBER: 130:57180
TITLE: Prolonged-release microcapsules comprising peptides and biodegradable polymers
INVENTOR(S): Pellet, Marc; Roume, Chantal
PATENT ASSIGNEE(S): Pharma Biotech S. A., Fr.
SOURCE: Fr. Demande, 16 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2762319	A1	19981023	FR 1997-4838	19970418

PRIORITY APPLN. INFO.: FR 1997-4838 19970418

AB Prolonged-release microcapsules comprising peptides and biodegradable polymers with intrinsic viscosity of 0.5-1.2 dL/g in CHCl3 and which the active ingredients are released up to 3 mo are disclosed. Thus, 16.620 g triptoreline acetate (I) was dissolved in 554 mL water and the solution was lyophilized. Then 3.378 g I was added to a solution of 7.30% polylactide-polyglycolide (inherent viscosity in CHCl3 = 0.7 dL/g) in dichloromethane. To above solution was added 390 mL silicone oil and the microcapsules thus formed were separated by immersion in heptane and filtered over a 10μm membrane.

IC ICM C07K007-06
ICS C07K007-00; C07K001-36; A61K038-09; A61K038-08; A61K009-52
CC 63-6 (Pharmaceuticals)
IT 50-56-6, Oxytocin, biological studies 58-82-2, Bradykinin 1066-17-7, Colistin 1393-25-5, Secretin 1404-26-8, Polymyxin B 1405-87-4, Bacitracin 1405-97-6, Gramicidin 1407-47-2, Angiotensin 9001-01-8, Kallikrein 9002-60-2, Adrenocorticotropic hormone, biological studies 9002-62-4, Prolactin, biological studies 9002-64-6, Parathyroid hormone 9002-67-9, Luteinizing hormone 9002-68-0, Follicle stimulating hormone 9002-71-5, Thyroid stimulating hormone 9002-76-0, Gastrin 9002-79-3, Melanocyte stimulating hormone 9004-10-8, Insulin, biological studies

9007-12-9, Calcitonin 9007-12-9D, Calcitonin, derivs. 9007-92-5, Glucagon, biological studies 9011-97-6, Pancreozymin 9015-68-3, Asparaginase 9034-39-3, Growth hormone releasing factor 9034-40-6, Lh-rh 9035-54-5 9039-53-6, Urokinase 9061-61-4, Nervegrowth factor 9063-57-4, Tuftsin 9066-59-5, Lysozyme hydrochloride 11000-17-2, Vasopressin 11096-26-7, Erythropoietin 11096-26-7D, Erythropoietin, analogs 17650-98-5, Caerulein 24305-27-9, Thyrotropin releasing hormone 26780-50-7 31362-50-2, Bombesin 33507-63-0, Substance p 37221-79-7, Vasoactive intestinal polypeptide 39379-15-2, Neurotensin 51110-01-1, Somatostatin 51110-01-1D, Somatostatin, analogs 52906-92-0, Motilin **53714-56-0**, Leuprorelin 57773-63-4, Triptoreline 57982-77-1, Buserelin 59392-49-3, Gastric inhibitory polypeptide 60118-07-2, Endorphin 60529-76-2, Thymopoietin 61512-21-8, Thymosin 62229-50-9, Epidermalgrowth factor 62683-29-8, Colony stimulating factor 65807-02-5, Goserelin 68893-82-3, Human Parathyroid hormone 70904-56-2, Kyotorphin 74913-18-1, Dynorphin 78310-77-7, Thymus factor X 127984-74-1, Lanreotide acetate 160296-12-8

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prolonged-release microcapsules comprising peptides and biodegradable polymers)

IT **53714-56-0**, Leuprorelin

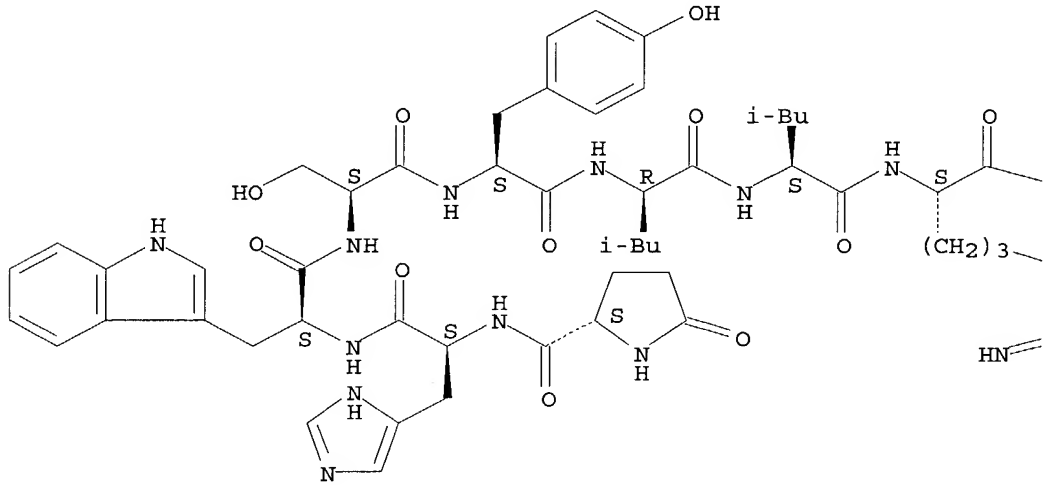
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prolonged-release microcapsules comprising peptides and biodegradable polymers)

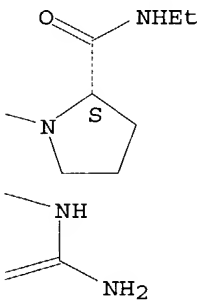
RN 53714-56-0 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A





L14 ANSWER 4 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:785345 CAPLUS
DOCUMENT NUMBER: 130:134499
TITLE: Leuprolide, a gonadotropin-releasing hormone agonist, enhances colonization after spermatogonial transplantation into mouse testes
AUTHOR(S): Ogawa, T.; Dobrinski, I.; Avarbock, M. R.; Brinster, R. L.
CORPORATE SOURCE: School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA, 19104-6009, USA
SOURCE: Tissue & Cell (1998), 30(5), 583-588
CODEN: TICEBI; ISSN: 0040-8166
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Spermatogonial stem cells can be transplanted from a fertile donor mouse to the testis of an infertile recipient where they establish spermatogenesis and produce spermatozoa. In the present study we investigated whether treatment of recipient mice with the gonadotropin-releasing hormone (GnRH) agonist leuprolide acetate could alter the efficiency of colonization by donor spermatogonial stem cells in the recipient testis. Six recipient mice were treated with busulfan to destroy endogenous spermatogenesis followed by injection of leuprolide acetate to three of the mice. Testis cells from mice carrying the ZFIacZ transgene, which produces β-galactosidase in spermatids, were used as donor cells for transplantation to allow for identification of donor spermatogenesis in the recipient testis by staining for enzyme activity. The extent of donor cell colonization was compared between leuprolide treated recipients and untreated control mice 3 mo after transplantation. Efficiency of colonization by donor cells was markedly enhanced in recipient mice treated with the GnRH agonist leuprolide acetate, which makes the technique of spermatogonial transplantation applicable to a wide range of exptl. situations. The present study also indicates that this technique can be used as a biol. assay system to investigate factors controlling the establishment and progression of spermatogenesis.

CC 2-10 (Mammalian Hormones)
IT **53714-56-0**, Leuprolide 74381-53-6, Leuprolide acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(leuprolide enhances colonization after spermatogonial transplantation

into mouse testes)

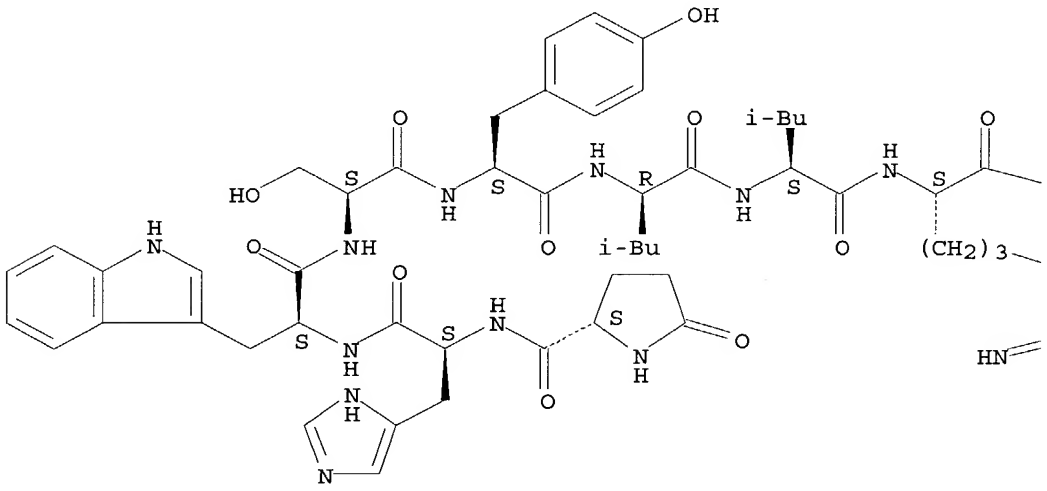
IT **53714-56-0**, Leuprolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(leuprolide enhances colonization after spermatogonial transplantation into mouse testes)

RN 53714-56-0 CAPLUS

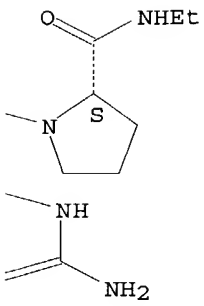
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:761097 CAPLUS

DOCUMENT NUMBER: 130:204727
TITLE: Treatment of patients with advanced prostate carcinoma with a luteinizing releasing hormone analog enatone
AUTHOR(S): Sun, Zhongquan; Hu, Baohua
CORPORATE SOURCE: Department of Urology, East China Hospital, Shanghai, 200040, Peop. Rep. China
SOURCE: Shanghai Yixue (1998), 21(8), 495-496
CODEN: SIHSD8; ISSN: 0253-9934
PUBLISHER: Shanghai Yixue Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB 20 Patients with advanced prostate carcinoma were received Yinatong, a extended releasing injection of LHRH synthetic analog leuprorelin, enatone, s.c. 3.75 mg therapy once every 4 wk, and addnl. flutamide 250 mg t.i.d. was initiated 3 days before the therapy and continued for at least 3 wk. The patients received enatone therapy 3-13 mo, all the 20 patients had their blood testosterone reduced to castrated level 4 wk after initiation of the therapy; 18/19 primary cases had their blood prostate specific antigen reduced to < 1.5 μg/L, a very low level, and one case remained at 20 μg/L, the 1 relapsed case was not reduced and remained >15 μg/L. 18 Patients had objective efficacy, 1 complete remission, with the tumor mass disappeared at rectal exam. (C stage), 17 cases had the tumor mass reduced 50% (13 C stage and 4 D stage), 1 stabilized (D stage), 1 worsened (D stage, relapsed); 15 patients had subjective efficacy, the symptoms of dysuria and metastasis bone pain ameliorated. 1 D stage relapsed patient was not responded to the therapy and died at the 6th month of therapy, another 1 C stage patient was died because of cerebral hemorrhage at the 8th month therapy. 4 Gastrointestinal reaction, 1 shoulder pain, 1 scrotum edema, and 1 gynecomastia were observed, impotency and sex desire alterations were not analyzed because of the patients were aged. The results suggest that the enatone as a LHRH analog, is effective and safe in treatment of advanced prostate cancer as it effectively reduced the patients blood testosterone; and the effect of initial raise of blood testosterone was blocked by administration of flutamide.

CC 1-6 (Pharmacology)
Section cross-reference(s): 2, 63

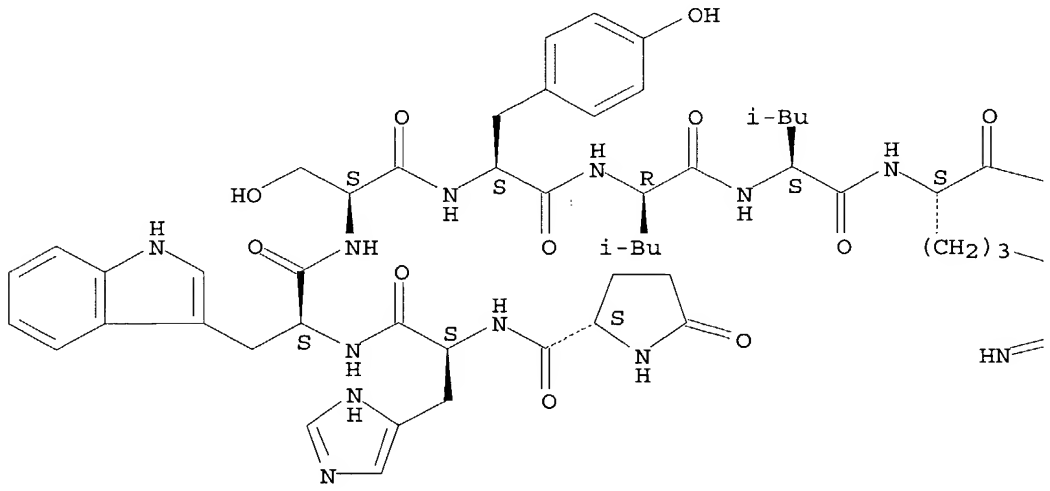
IT **53714-56-0**, Leuprorelin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enatone; treatment of patients with advanced prostate carcinoma with a luteinizing releasing hormone analog enatone)

IT **53714-56-0**, Leuprorelin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enatone; treatment of patients with advanced prostate carcinoma with a luteinizing releasing hormone analog enatone)

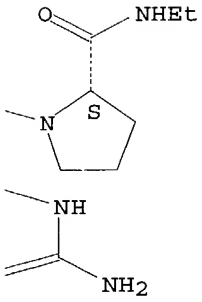
RN 53714-56-0 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



L14 ANSWER 6 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:755435 CAPLUS
DOCUMENT NUMBER: 130:148890
TITLE: Treatment of hirsutism by gonadotropin-releasing hormone agonist (GnRH-A), finasteride and flutamide in women with polycystic ovary syndrome
AUTHOR(S): Falsetti, L.; Rosina, B.; Martini, P.
CORPORATE SOURCE: Department of Gynecologic Endocrinology, University of Brescia, Brescia, Italy
SOURCE: Infertility and Assisted Reproductive Technology: From Research to Therapy, Proceedings of the International Meeting on Infertility and Assisted Reproductive Technology: From Research to Therapy, Porto Cervo, Italy, June 11-14, 1997 (1997), 433-438. Editor(s): Ambrosini, Antonio. Monduzzi Editore: Bologna, Italy.

CODEN: 66ZUAV
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The object of this study was to evaluate the efficacy of gonadotropin-releasing hormone agonist (GnRH-A), Finasteride and Flutamide in the treatment of hirsutism in women with polycystic ovary syndrome (PCOS). Sixty-two women with PCOS and hirsutism were randomly treated for six consecutive months with GnRH-A (Leuprolide), Finasteride (Prostide) and Flutamide (Eulexin). The Ferriman and Gallway score (F.G. score) and hair diameter were monitored. In 6 mo GnRH-A, Finasteride and Flutamide significantly decreased the F.G. score by 22%, 25% and 22% resp. Hair diameter significantly decreased with GnRH-A by 28-34%, with Finasteride by 19-25% and with Flutamide by 21-22%. Side effects of this therapy include hot flashes, sweating, headache, vaginal dryness, and bone demineralization.

CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 1

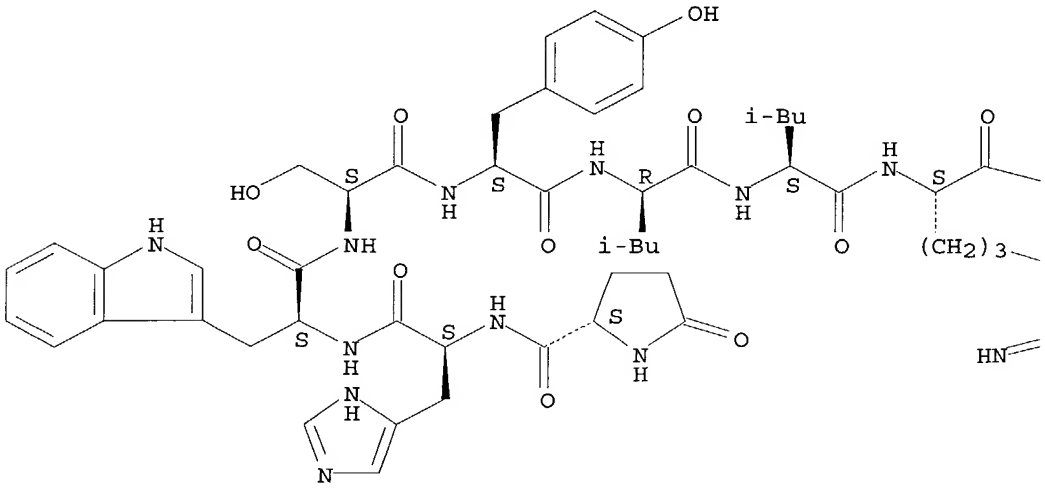
IT 13311-84-7, Eulexin **53714-56-0**, Leuprolide 98319-26-7, Prostide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gonadotropin-releasing hormone agonist, finasteride and flutamide for treatment of hirsutism in women with polycystic ovary syndrome)

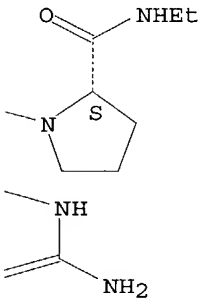
IT **53714-56-0**, Leuprolide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gonadotropin-releasing hormone agonist, finasteride and flutamide for treatment of hirsutism in women with polycystic ovary syndrome)

RN 53714-56-0 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A





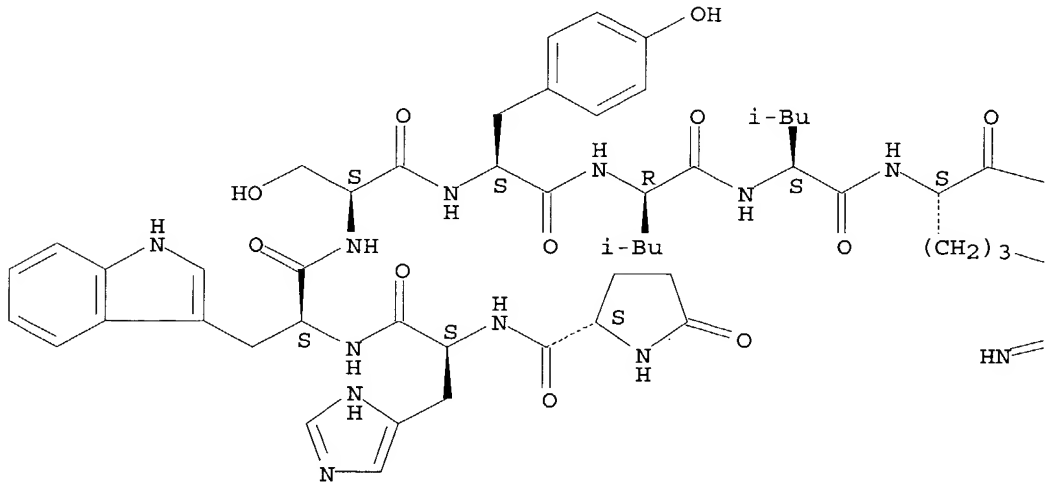
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:754776 CAPLUS
DOCUMENT NUMBER: 130:136961
TITLE: The effect of different GnRH analogs in inducing spawning in Rana rugulosa
AUTHOR(S): Nootprapan, T.; Pariyanonth, P.; Werawatgoompa, S.; Krogstad, A.
CORPORATE SOURCE: Department of Biology, Faculty of Science, Chulalongkorn University, Bangkok, Thailand
SOURCE: Advances in Comparative Endocrinology, Proceedings of the International Congress of Comparative Endocrinology, 13th, Yokohama, Nov. 16-21, 1997 (1997), Volume 1, 725-728. Editor(s): Kawashima, Seiichiro; Kikuyama, Sakae. Monduzzi Editore: Bologna, Italy. CODEN: 66ZWA3
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Three synthetic analogs of gonadotropin releasing hormone (GnRH), D-Ala6,Pro9 ethylamide-LHRH, D-Leu6,Pro9-ethylamide-LHRH and D-Ser6,Pro9-ethylamide-LHRH (Buserelin) induced spawning behavior in both sexes of Rana rugulosa. The analog Buserelin produced a higher rate of spawning and fertilization (41.45 %) than did D-Ala6,Pro9-ethylamide-LHRH (fertilization rate 21.0 %) and D-Leu6,Pro9-ethylamide-LHRH (fertilization rate 11.0 %).
CC 12-6 (Nonmammalian Biochemistry)
IT 9034-40-6D, LH-RH, analogs 52435-06-0 **53714-56-0** 57982-77-1, Buserelin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(LH-RH analogs effect on spawning and fertilization rate in Rana rugulosa)
IT **53714-56-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(LH-RH analogs effect on spawning and fertilization rate in Rana rugulosa)
RN 53714-56-0 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-

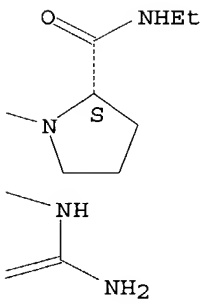
prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:744003 CAPLUS
DOCUMENT NUMBER: 130:148840
TITLE: Suppression of plasma gonadotropins by abarelix: a potent new LHRH antagonist
AUTHOR(S): Molineaux, Christopher J.; Sluss, Patrick M.; Bree, Mark P.; Gefter, Malcolm L.; Sullivan, Leah M.; Garnick, Marc B.
CORPORATE SOURCE: PRAECIS Pharmaceuticals, Inc., Cambridge, MA, USA
SOURCE: Molecular Urology (1998), 2(3), 265-269

CODEN: MOURFE; ISSN: 1091-5362
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Abarelix (PPI-149) is the decapeptide N-Ac-D-Nal(2)-D-pCl-Phe-D-Pal(3)-Ser-NM-Tyr-Asn-Leu-ILys-Pro-Gly-NH2. This compound is a novel, potent competitive LH-releasing hormone (LHRH) antagonist with a high water solubility and low induction of histamine release. Abarelix administered via continuous infusion induces a rapid decrease in the plasma concentration of testosterone that is maintained throughout the course of administration of the antagonist. The drop in plasma testosterone is accompanied by a corresponding decrease in the plasma levels of the gonadotropins LH and FSH. The LHRH agonists currently used in the treatment of prostate cancer induce a large increase in plasma levels of gonadotropins and gonadal steroids prior to downregulating pituitary gonadotropin secretion. This study compares the initial stimulatory effects of the LHRH agonist leuprolide in rats with the rapid suppression of plasma testosterone, LH, and FSH induced by abarelix.

CC 2-4 (Mammalian Hormones)

IT **53714-56-0**, Leuprolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(comparison with; suppression of plasma gonadotropins by abarelix, potent LHRH antagonist)

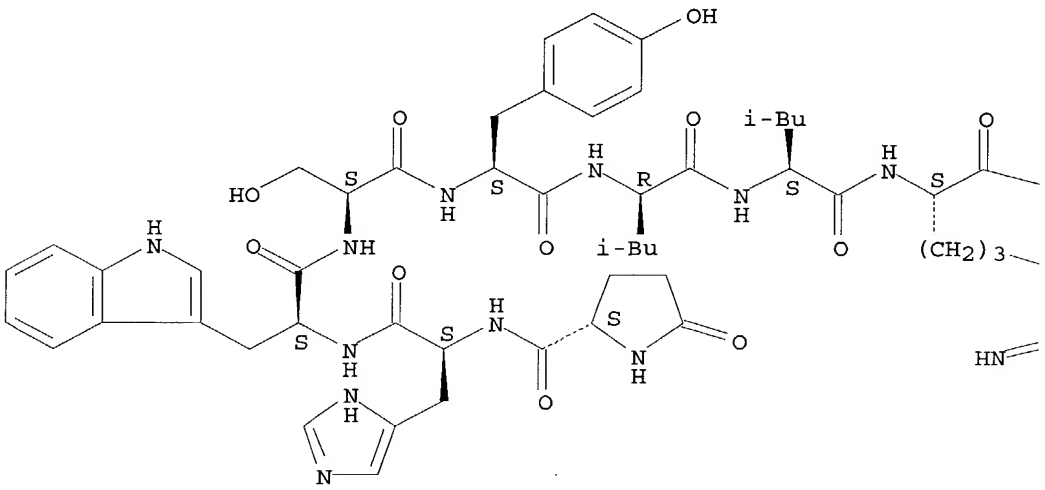
IT **53714-56-0**, Leuprolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(comparison with; suppression of plasma gonadotropins by abarelix, potent LHRH antagonist)

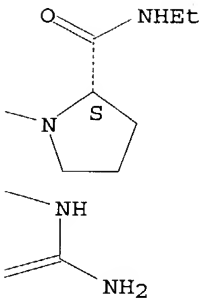
RN 53714-56-0 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A





REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:743986 CAPLUS
DOCUMENT NUMBER: 130:134283
TITLE: Neoadjuvant androgen suppression and permanent radioactive seed implantation in the treatment of stage T1-T2 prostate cancer
AUTHOR(S): Stock, Richard G.; Stone, Nelson N.; Yeghiayan, Paula
CORPORATE SOURCE: Department of Radiation Oncology, Mount Sinai School of Medicine, New York, NY, USA
SOURCE: Molecular Urology (1998), 2(3), 121-127
CODEN: MOURFE; ISSN: 1091-5362
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Neoadjuvant androgen suppression (NAS) and brachytherapy have emerging roles in the treatment of prostate cancer. Although NAS has been used with external-beam irradiation and radical prostatectomy, there is little information on its use with brachytherapy. The authors describe the authors' experience with NAS and permanent radioactive seed implantation to assess the impact on prostate volume and prostate specific antigen (PSA) changes, biopsy results, and morbidity. Neoadjuvant androgen suppression was given prior to radioisotope implantation in 76 patients with prostate vols. >50 Cm3 (N = 13), or Gleason score ≥7, PSA >10 ng/mL, or stage T2c disease (N = 63). Hormonal therapy was accomplished with 3 mo of leuprolide and flutamide prior to and 2 mo after seed implantation. All patients received 103Pd seeds to a dose of 115 Gy. Presenting PSA values ranged from 4.0 to 57.0 ng/mL (median 11 ng/mL; mean 14.4 ng/mL). Gleason scores were 2-4 in 16 patients (21%), 5-6 in 28 patients (37%), and 7 or greater in 32 patients (42%). The clin. stage was T1b in 1 patient, T1c in 15 patients (20%), T2a in 16 patients (21%), T2b in 25 patients (33%), and T2c in 19 patients (25%). Prostate volume measurements were taken using transrectal ultrasonog. prior to administration of NAS for 61 patients and ranged from 17.2 to 118.3 Cm3 (median 45.5 Cm3; mean 50.16 Cm3). Follow-up ranged from 12 to 65 (median 20) months. The median change in prostate volume after NAS and prior to implantation was a decrease to 60% of the baseline volume After this decrease in volume, prostate vols. remained stable throughout the follow-up period and after cessation of NAS. The actuarial freedom from biochem. failure at 4 yr (PSA ≤1 ng/mL) was 78%. Pretreatment prognostic factors, PSA,

stage, and Gleason score had no significant effect on the likelihood of biochem. failure. Neg. 2-yr post-treatment prostate biopsies were obtained in 23 of 24 patients (96%). The actuarial preservation of sexual potency at 2 yr was 54%. There were no cases of late bladder or rectal complications. Urinary retention necessitating Foley catheterization occurred in 12% and led to transurethral resection of the prostate in 7%. When given prior to 103Pd brachytherapy, NAS can help reduce prostate volume, and the combined therapy results in relatively high biochem. control rates and neg. post-treatment biopsy results in a group of patients with high-risk features. Although the therapy is associated with low morbidity, it is also associated with a lower preservation of sexual potency than seed implants alone.

CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 8

IT 13311-84-7, Flutamide **53714-56-0**, Leuprolide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoadjuvant androgen suppression and permanent radioactive seed implantation in treatment of stage T1-T2 prostate cancer in humans)

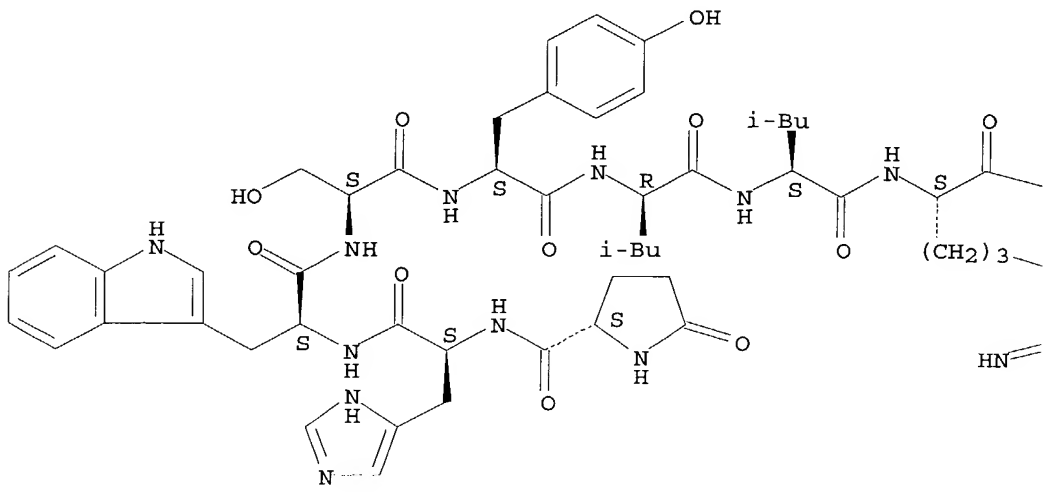
IT **53714-56-0**, Leuprolide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoadjuvant androgen suppression and permanent radioactive seed implantation in treatment of stage T1-T2 prostate cancer in humans)

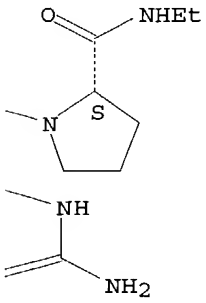
RN 53714-56-0 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A





REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:690537 CAPLUS
DOCUMENT NUMBER: 130:105421
TITLE: Time to normalization of serum testosterone after 3-month luteinizing hormone-releasing hormone agonist administered in the neoadjuvant setting: implications for dosing schedule and neoadjuvant study consideration
AUTHOR(S): Oefelein, Michael G.
CORPORATE SOURCE: 74th Medical Group/SGOSU, Wright-Paterson Air Force Base, OH, USA
SOURCE: Journal of Urology (Baltimore) (1998), 160(5), 1685-1688
CODEN: JOURAA; ISSN: 0022-5347
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A time course to serum testosterone normalization after administration of a single 3-mo LH-releasing hormone (LH-RH) agonist in the neoadjuvant setting was developed. A total of 13 men with clin. localized prostate cancer were prospectively assessed for baseline libido, erectile function and mid morning serum testosterone. A single 3-mo formulation LH-RH agonist was administered in the neoadjuvant setting before definitive treatment with radical perineal prostatectomy in 7 men or external beam radiotherapy in 6. Baseline and serial testosterone levels were measured 3, 4, 6, 7, 9, 12, 15 and 18 mo after injection. Symptoms related to acute testosterone depletion, namely hot flashes and sweats, were recorded on the same schedule. After a single 3-mo LH-RH agonist injection median duration of castrate level testosterone (0.2 ng./mL. or less) was 6 mo. Median duration of hypogonadal symptoms (hot flashes and sweats) was 13.6 mo and resolution paralleled the gradual return of serum testosterone to baseline values. The 3-mo formulation of LH-RH agonist administered in the neoadjuvant setting provides castrate level testosterone for a longer duration than the product labeling suggests. If confirmed, these preliminary observations have important implications for dosing schedule and neoadjuvant study consideration.

CC 2-4 (Mammalian Hormones)
IT **53714-56-0**, Leuprolide 65807-02-5, Goserelin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(time to normalization of serum testosterone after 3-mo LH-RH neoadjuvant treatment in prostate cancer in men)

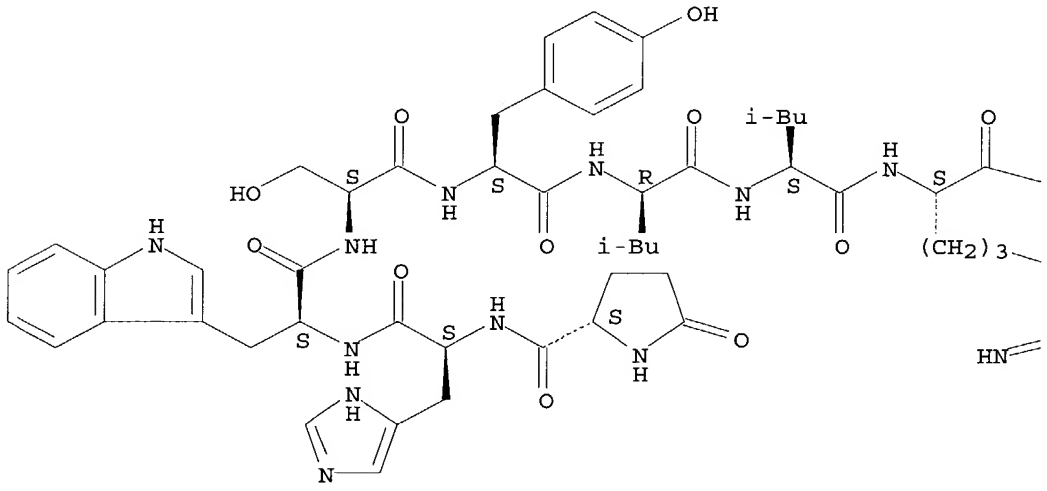
IT **53714-56-0**, Leuprolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(time to normalization of serum testosterone after 3-mo LH-RH neoadjuvant treatment in prostate cancer in men)

RN 53714-56-0 CAPLUS

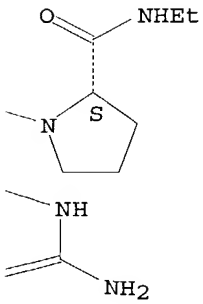
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



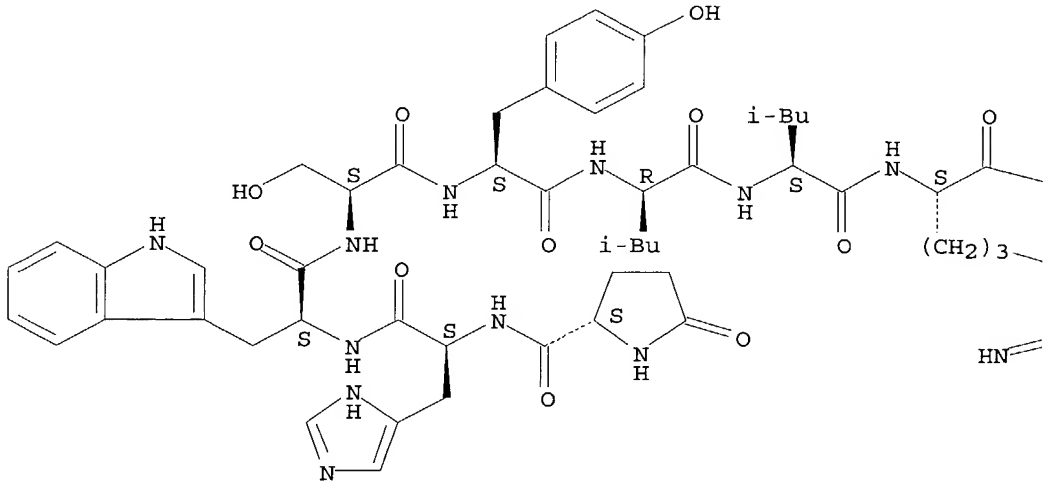
L14 ANSWER 11 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:668493 CAPLUS
DOCUMENT NUMBER: 129:280813
TITLE: Efficacy, safety, and mechanism of cyclodextrins as absorption enhancers in nasal delivery of peptide and protein drugs
AUTHOR(S): Marttin, E.; Verhoef, J. C.; Merkus, F. W. H. M.
CORPORATE SOURCE: Department Pharmaceutical Technology Biopharmaceutics, Leiden/Amsterdam Center Drug Research, Leiden, 2300 RA, Neth.
SOURCE: Journal of Drug Targeting (1998), 6(1), 17-36
CODEN: JDTAEH; ISSN: 1061-186X
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB Cyclodextrins are used in nasal drug delivery as absorption enhancing compds. to increase the intranasal bioavailability of peptide and protein drugs. The most effective cyclodextrins in animal expts. are the methylated derivs., dimethyl-β-cyclo-dextrin and randomly methylated β-cyclodextrin, which are active at low concns. ranging between 2% and 5%. However, large species differences between rats, rabbits and humans exist for the nasal absorption enhancement by cyclodextrins. Based on toxicol. studies of the local effects of cyclodextrins on the nasal mucosa dimethyl-β-cyclodextrin and randomly methylated β-cyclodextrin are considered safe nasal absorption enhancers. Their effects were quite similar to controls (physiol. saline), but smaller than those of the preservative benzalkonium chloride in histol. and ciliary beat frequency studies. In these studies, and in a study of the release of marker compds. after nasal administration, methylated β-cyclodextrins were less toxic than sodium glycocholate, sodium taurodihydrofusidate, laureth-9 and L-α-phosphatidylcholine. Systemic toxicity after nasal cyclodextrin administration is not expected, because very low doses of cyclodextrins are administered and only very small amts. are absorbed. The mechanism of action of cyclodextrins may be explained by their interaction with the nasal epithelial membranes and their ability to transiently open tight junctions. This article is reviewed by many refs.

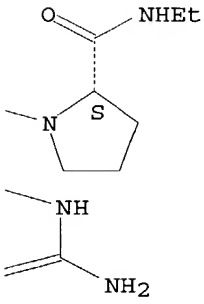
CC 63-0 (Pharmaceuticals)
IT 9002-60-2, ACTH, biological studies 9004-10-8, Insulin, biological studies 9007-12-9, Calcitonin 9007-92-5, Glucagon, biological studies 10016-20-3, α-Cyclodextrin 17465-86-0, γ-Cyclodextrin 51166-71-3, Dimethyl-β-cyclodextrin **53714-56-0**, Leuprolide 57982-77-1, Buserelin 121181-53-1
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy, safety, and mechanism of cyclodextrins as absorption enhancers in nasal delivery of peptide and protein drugs)
IT **53714-56-0**, Leuprolide
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy, safety, and mechanism of cyclodextrins as absorption enhancers in nasal delivery of peptide and protein drugs)
RN 53714-56-0 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



L14 ANSWER 12 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:618291 CAPLUS
DOCUMENT NUMBER: 129:321073
TITLE: Effect of gelation on the chemical stability and conformation of leuprolide
AUTHOR(S): Tan, Mandy M.; Corley, Cynthia A.; Stevenson, Cynthia L.
CORPORATE SOURCE: Biopharmaceutical R and D. ALZA Corporation, Palo Alto, CA, 94303, USA
SOURCE: Pharmaceutical Research (1998), 15(9), 1442-1448
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to characterize the conformation,

aggregation, and stability of leuprolide on gelation. FTIR spectra of leuprolide solns. and gels were collected in water, propylene glycol (PG), DMSO, and trifluoroethanol (TFE) leuprolide solution and gel stability data were obtained by SEC and RP-HPLC. Leuprolide was induced to gel with increasing peptide concentration, introduction of salts, and gentle agitation. Leuprolide dissolved in water (400 mg/mL) demonstrated FTIR spectra consisting of two major bands of equal intensity at 1615 cm-1 and 1630 cm-1, similar to inter- and intra-mol. β-sheet structure in proteins. When samples were gently agitated for 24 h at 25°, the formulation was observed to change from a viscous liquid to an opaque gel with a concomitant shift in IR spectra from the equal intensity bands to mostly 1630 cm-1, indicating a shift to a preferred β-sheet structure. Incubation of leuprolide with 20-200 mM salts at 25° and 37° also produced gels ranging from clear to cloudy and stringy white ppts. The gel and precipitate were marked by a shift of the predominant β-sheet band to 1630 cm-1 and 1615 cm-1, resp. Leuprolide was also observed to gel and/or precipitate in mixts. of water, PG or TFE, but not in DMSO.

Birefringence

was noted in many of the firmer gels. Both solns. and gels demonstrated minimal dimer or trimer formation, with no larger order aggregates detected. The chemical stability profile of gelled leuprolide was similar to that of the non-gelled water formulation by RP-HPLC.

CC 63-5 (Pharmaceuticals)

IT **53714-56-0**, Leuprolide

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(gelation effect on stability and conformation of leuprolide)

IT **53714-56-0**, Leuprolide

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

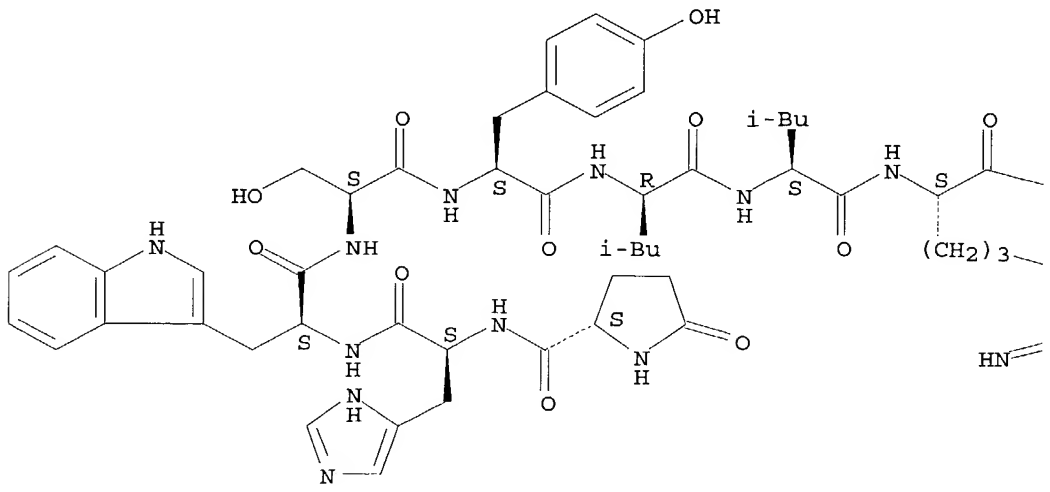
(gelation effect on stability and conformation of leuprolide)

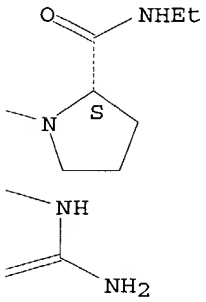
RN 53714-56-0 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A





REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 13 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:542029 CAPLUS
DOCUMENT NUMBER: 129:285668
TITLE: A randomized comparison of the clinical and hormonal effects of two GnRH agonists in patients with prostate cancer
AUTHOR(S): Kuhn, J. M.; Abourachid, H.; Brucher, P.; Doutres, J. C.; Fretin, J.; Jaupitre, A.; Jorest, R.; Lambert, D.; Petit, J.; Pin, J.; Blumberg, J.; Dufour-Esquerre, F.
CORPORATE SOURCE: Department of Endocrinology, CHU of Rouen, Rouen, F-76031, Fr.
SOURCE: European Urology (1997), 32(4), 397-403
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aims of the study were (i) to compared the efficacy of the two long-acting GnRH agonists (GnRHa) triptorelin (Trp) and leuprolide (Leu) in men with prostate cancer and (ii) to assess the pattern of plasma testosterone levels following each injection of GnRHa. 67 Patients referred for prostate cancer not suitable for surgery were randomly allocated to two treatment regimens: 33 patients received 3.75 mg Trp i.m. at 4-wk intervals for 3 mo and 34 patients were treated with 3.75 mg Leu s.c. at the same rhythm of administration for 3 mo. Clin. data at entry and assessed monthly during follow-up did not differ between the two groups. Plasma prostate-specific antigen (PSA) and testosterone were measured before, 24 and 72 h after each injection of GnRHa. During treatment, PSA dropped similarly in both groups. By month 2, testosterone was <1.0 nmol/l in 77 and 48% of patients treated with Trp and Leu, resp. ($p = 0.02$). 24 And 72 h after GnRHa injection, 77 (Trp) and 56% (Leu) of patients had testosterone <1.0 nmol/l ($p < 0.05$). The second and third injections of GnRHa were not followed by a significant increase in testosterone. Trp induced a higher decrease in testosterone than did Leu. The implications in terms of survival should, however, be studied in a larger and longer study.

CC 1-6 (Pharmacology)
Section cross-reference(s): 2

IT **53714-56-0**, Leuprolide 57773-63-4, Triptorelin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leuprolide vs. triptorelin clin. and hormonal effects in humans with prostate cancer)

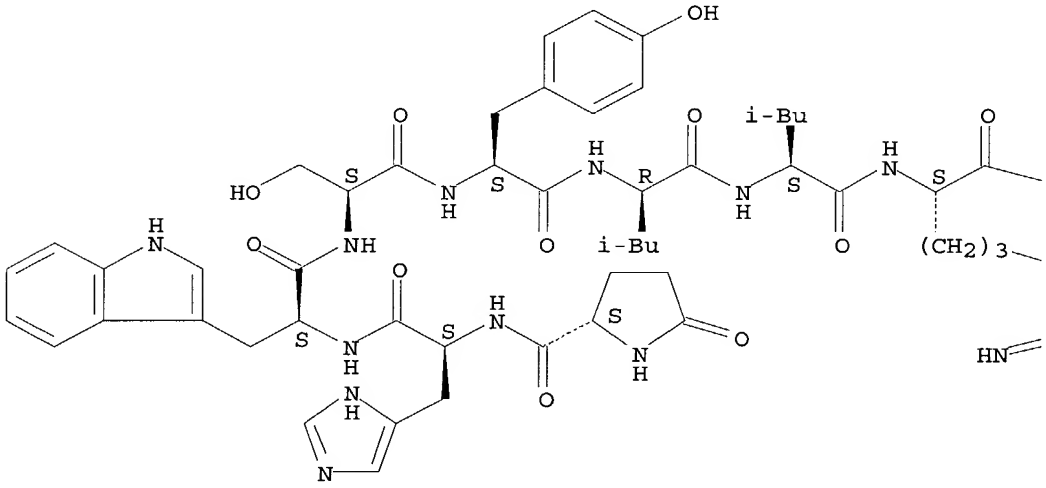
IT **53714-56-0**, Leuprolide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leuprolide vs. triptorelin clin. and hormonal effects in humans with prostate cancer)

RN 53714-56-0 CAPLUS

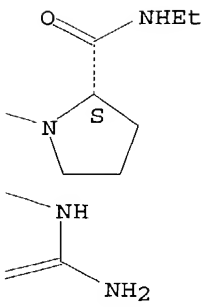
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 14 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:542014 CAPLUS
DOCUMENT NUMBER: 129:288459
TITLE: Promoting effects and mechanisms of action of androgen in bladder carcinogenesis in male rats
AUTHOR(S): Imada, Seiki; Akaza, Hideyuki; Ami, Yoshihiro; Koiso, Kenkichi; Ideyama, Yukitaka; Takenaka, Toichi
CORPORATE SOURCE: Department of Urology, Institute of Clinical Medicine, University of Tsukuba, Tsukuba, Japan
SOURCE: European Urology (1997), 31(3), 360-364
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has been reported that blocking of testosterone production inhibits bladder carcinogenesis in various animal models. The authors investigated how testosterone acts on rat bladder carcinogenesis using an antiandrogen, flutamide, and a 5α-reductase inhibitor, finasteride. Experiment 1: the authors administered 0.05% BBN [N-butyl-N-(4-hydroxybutyl)nitrosamine] orally to 117 Wistar rats for 10 wk, divided them into seven groups - control, surgical castration, finasteride (2 mg/kg), LH releasing hormone (LH-RH) agonist (1 mg/kg) flutamide (50 mg/kg), LH-RH agonist plus finasteride, and LH-RH agonist plus flutamide -, and then cystectomized them to investigate the incidence of bladder cancer on week 21; experiment 2: the authors administered 0.05% BBN to 154 Wistar rats for 7 wk, divided them into seven groups - control, finasteride 2, 4, and 8 mg/kg, and flutamide 50, 100, and 200 mg/kg -, and then the authors cystectomized them to investigate the dose-dependent influence on bladder carcinogenesis of these drugs on week 20, and experiment 3: the authors investigated the presence of androgen receptors in rat and mouse normal bladder mucosa using a monoclonal antibody. Experiment 1: Surgical castration and LH-RH agonist treatment significantly reduced the occurrence of carcinomas. There was no significant additive effect of coadministered finasteride or flutamide with LH-RH agonist. Finasteride or flutamide monotherapy showed no statistically significant effects on the results of experiment 1 at the doses used. Experiment 2: Flutamide showed a dose-dependent effect on reducing the number of rats with bladder cancer, and at a dose of 200 mg/kg twice a week, the difference was statistically significant when compared with the control group, whereas finasteride had no statistically significant suppressing effect at any dose. Experiment 3: Mouse and rat bladder urothelium expressed the androgen receptor. The authors' results indicate that testosterone itself might have a more potent action on bladder carcinogenesis rather than its converting form, 5α-dihydrotestosterone.

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1, 2

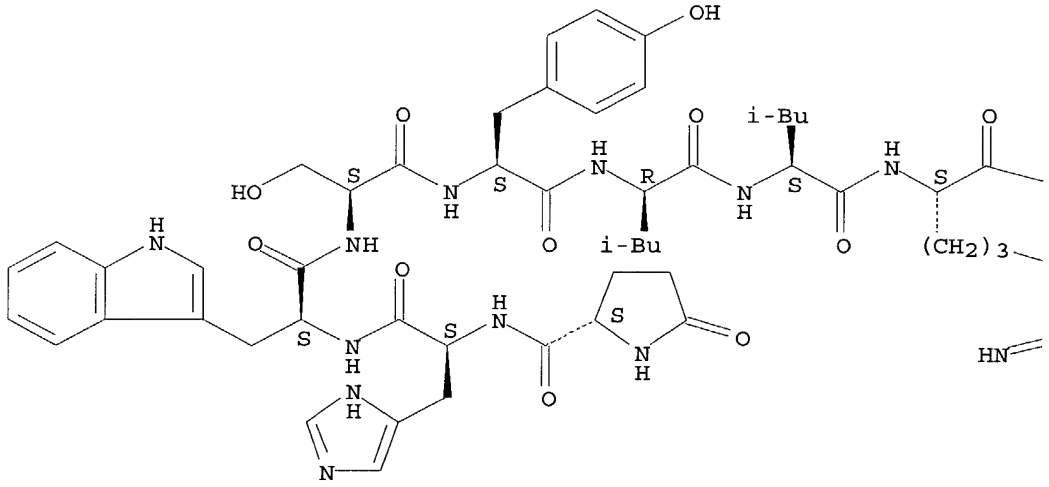
IT 13311-84-7, Flutamide **53714-56-0**, Leuprolide 98319-26-7, Finasteride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(androgen promoting effects and mechanisms of action in bladder carcinogenesis in male rats)

IT **53714-56-0**, Leuprolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological

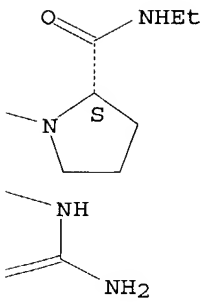
study); USES (Uses)
(androgen promoting effects and mechanisms of action in bladder carcinogenesis in male rats)
RN 53714-56-0 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 15 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:527189 CAPLUS
DOCUMENT NUMBER: 129:166217
TITLE: Sustained-release microspheres, their production and use

INVENTOR(S): Kamei, Shigeru; Ohta, Tsutomu; Saikawa, Akira; Igari, Yasutaka
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9832423	A1	19980730	WO 1998-JP339	19980128
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9856783	A1	19980818	AU 1998-56783	19980128
JP 10273447	A2	19981013	JP 1998-14698	19980128

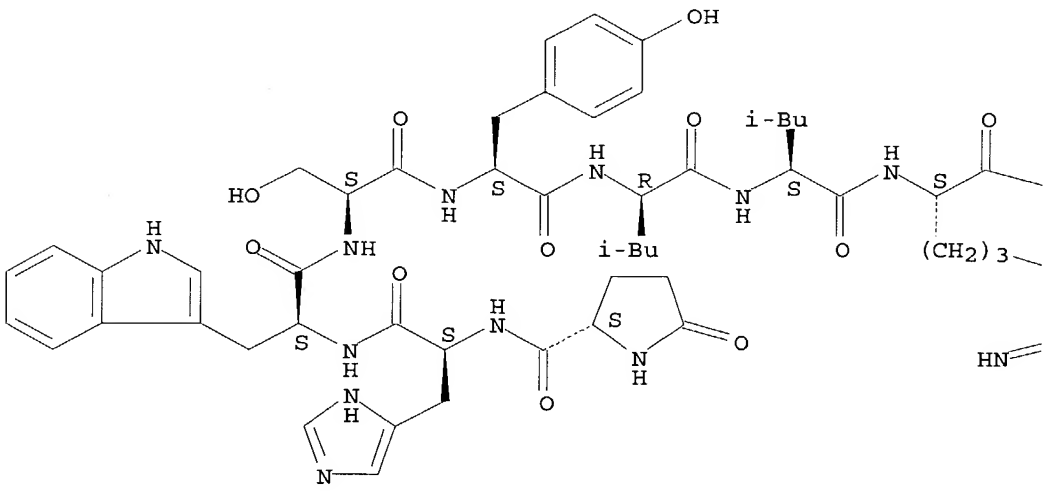
PRIORITY APPLN. INFO.: JP 1997-15203 19970129
WO 1998-JP339 19980128

AB The present invention provides a method of producing a sustained-release microsphere which comprises emulsification, a physiol. active peptide and a pamoic acid by a biodegradable polymer; a sustained-release microsphere comprising an about 0.01 to about 10 μm particle size of a pamoic acid salt of physiol. active peptide and a biodegradable polymer; a sustained-release microsphere comprising a complex or a salt formed by a physiol. active peptide, a pamoic acid or a salt thereof and a biodegradable polymer; and a sustained-release preparation comprising the microsphere. The microsphere contains a large amount of the physiol. active peptide and can regulate a release rate of the physiol. peptide. A solution of pamoic acid and N-(S)-2-tetrahydrofuroyl-Gly-D2Na1-D4ClPhe-D3Pal-Ser-NMeTyr-DLys(Nic)-Leu-Lys(Nisp)Pro-DAlaNH2 was encapsulated in lactic acid-glycolic acid copolymer microspheres.

IC ICM A61K009-16
ICS A61K009-50; A61K047-12; A61K038-00
CC 63-6 (Pharmaceuticals)
IT 130-85-8, Pamoic acid 6640-22-8, Disodium pamoate 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 34346-01-5, Glycolic acid-lactic acid copolymer **53714-56-0** 135215-95-1 168395-24-2 211108-59-7
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(sustained-release microspheres containing active peptide and pamoic acid derivative)
IT **53714-56-0**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(sustained-release microspheres containing active peptide and pamoic acid derivative)
RN 53714-56-0 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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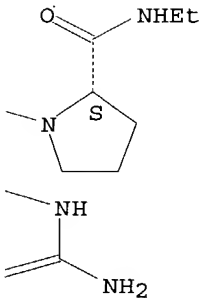


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 16 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:481911 CAPLUS
DOCUMENT NUMBER: 129:250169
TITLE: DUROS leuprolide implant for continuous one-year treatment of prostate cancer
AUTHOR(S): Wright, J.; Chen, G.; Cukierski, M.; Davis, C.; Falender, C.; Mabanglo, D.; Peery, J.; Ponnekanti, L.; Skowronski, R.; Stevenson, C.; Tao, S.; Brown, J.
CORPORATE SOURCE: ALZA Corporation, Palo Alto, CA, 94303, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1998), 25th, 516-517
CODEN: PCRMEY; ISSN: 1022-0178

PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A 1-yr duration osmotic delivery implant was developed for the delivery of leuprolide for the palliative treatment of prostate cancer. The implant system (consisting of a cylindrical Ti alloy drug reservoir that is capped at 1 end by a rate-controlling semipermeable membrane) successfully reduced testosterone levels in dogs.

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

IT **53714-56-0**, Leuprolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DUROS leuprolide implant for continuous treatment of prostate cancer)

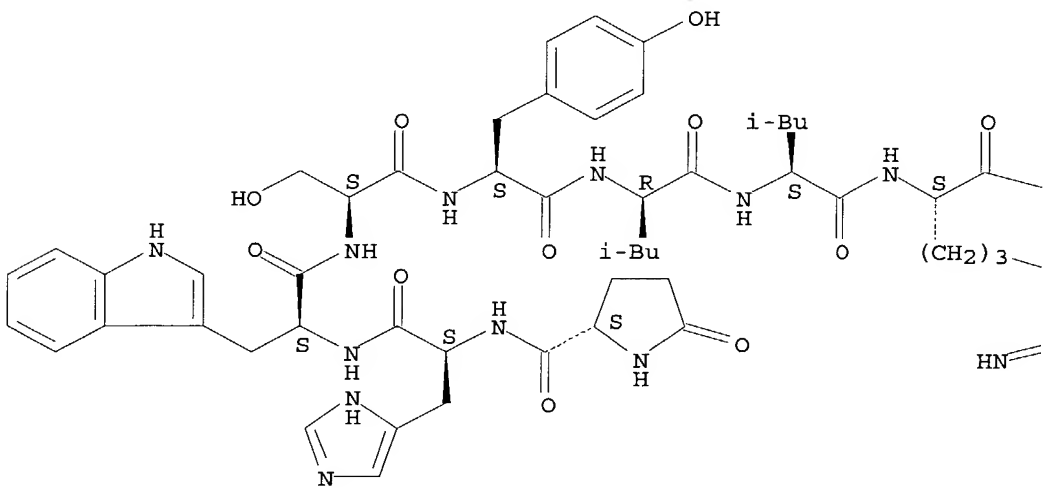
IT **53714-56-0**, Leuprolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DUROS leuprolide implant for continuous treatment of prostate cancer)

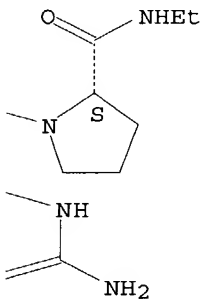
RN 53714-56-0 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A





REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 17 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:423424 CAPLUS
DOCUMENT NUMBER: 129:198217
TITLE: Fas and fas ligand system may mediate antiproliferative activity of gonadotropin-releasing hormone receptor in endometrial cancer cells
AUTHOR(S): Imai, Atsushi; Takagi, Atsushi; Horibe, Shinji; Takagi, Hiroshi; Tamaya, Teruhiko
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Gifu University School of Medicine, Gifu, 500-8705, Japan
SOURCE: International Journal of Oncology (1998), 13(1), 97-100
CODEN: IJONES; ISSN: 1019-6439
PUBLISHER: International Journal of Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Gonadotropin-releasing hormone (GnRH) receptor-bearing tumors undergo apoptosis in vivo and in vitro with GnRH analogs. The authors recently showed that GnRH stimulation induces intratumoral expression of the apoptosis-inducing Fas ligand in human reproductive tract tumors. To provide a potential association of Fas/Fas ligand system with the antiproliferative signaling process of GnRH receptor, the authors evaluated a correlation between the Fas ligand expression and the number of viable cells in two types of GnRH receptor-bearing endometrial carcinomas that differ in Fas content. Surgically removed uterine endometrial carcinomas had been screened for the presence of GnRH receptor and Fas before analyses. Fas ligand protein was characterized by immunoblotting of membrane proteins with the specific antibody. After a lag time of 2 days, incubation with a GnRH analog leuprolide (10 μM) induced significant growth inhibition of the Fas- and GnRH receptor-bearing cells. Time course anal. showed that Fas ligand production, which was already observed at day 2, precedes the onset of reduction in viable cell number The stimulatory effect of GnRH on Fas ligand expression and reduction of viable cells revealed dose-dependency. The analog at concentration of 10 μM induced up to 90% reduction in cell number In contrast, the growth of Fas-neg. cells was not affected by the analog, although Fas ligand appeared in response to the GnRH analog.

These data demonstrate that the co-presence of Fas could be essential for GnRH to promote antiproliferative action in endometrial cancer cells carrying GnRH receptor. The hormone may act through intratumor Fas and Fas ligand system to induced growth inhibition in GnRH-sensitive tumors.

CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 14

IT **53714-56-0**, Leuprolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Fas and Fas ligand system may mediate antiproliferative activity of gonadotropin-releasing hormone receptor in endometrial cancer cells)

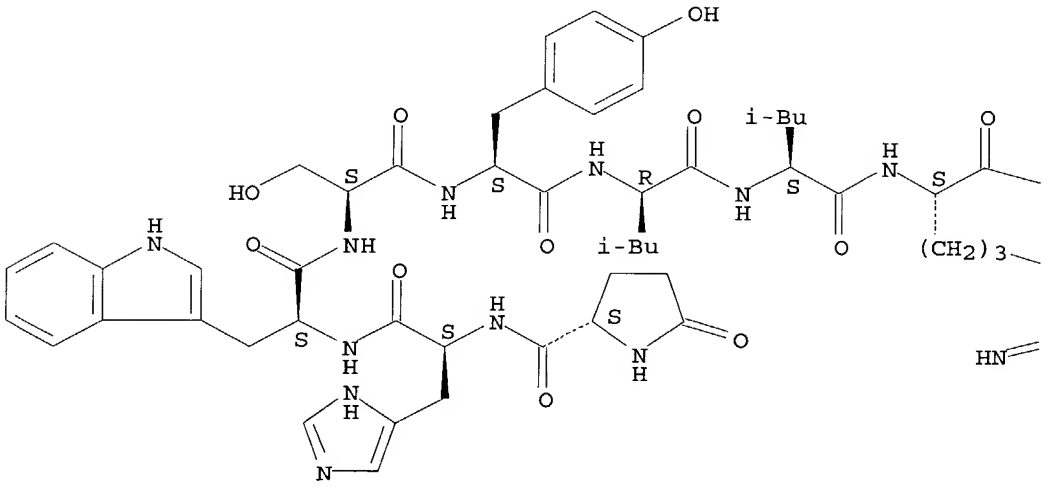
IT **53714-56-0**, Leuprolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Fas and Fas ligand system may mediate antiproliferative activity of gonadotropin-releasing hormone receptor in endometrial cancer cells)

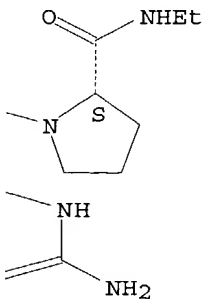
RN 53714-56-0 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A





REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 18 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:416563 CAPLUS
DOCUMENT NUMBER: 129:130619
TITLE: Sensitive reversed-phase liquid chromatographic determination of fluoride based on its ternary systems with zirconium(IV) or hafnium(IV) and 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol
AUTHOR(S): Oszwaldowski, Slawomir; Lipka, Robert; Jarosz, Maciej; Majewski, Tadeusz
CORPORATE SOURCE: Department of Analytical Chemistry, Faculty of Chemistry, Warsaw University of Technology, Warsaw, 00-664, Pol.
SOURCE: Analyst (Cambridge, United Kingdom) (1998), 123(7), 1529-1533
CODEN: ANALAO; ISSN: 0003-2654
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Optimum conditions for the direct reversed-phase LC determination of fluoride based on the ternary M-F--(5-Br-PADAP) complexes [M = ZrIV or HfIV and 5-Br-PADAP = 2-(5-bromo-2-pyridylazo)- 5-diethylaminophenol] were evaluated. Chromatog. separation was performed with C18 end-capped column with an eluent consisting of MeCN-H2O (85 +15 volume/volume) mixture of pH 4.0 ± 0.3 (flow rate 1 mL min-1), the eluate was monitored spectrophotometrically at λmax = 585 nm. The calibration curves were linear over a wide range of fluoride concns.: from 1 to 110 and 150 ng ml-1 for the ZrIV-F--(5-Br-PADAP) and HfIV-F--(5-Br-PADAP) systems, resp. (using a 20 μL loop). Under such conditions the detection limits were 0.8 and 0.7 ng ml-1, resp., and the quantification limit is 1.0 ng ml-1 for both methods. When a 100 μL loop was used, the limits of both detection and quantification in the method based on the Zr system were 0.2 ng ml-1. Using the proposed method, fluoride was determined directly in tap H2O, saliva and an anti-cancer agent for prostatic cancer (Leuprolid).

CC 79-6 (Inorganic Analytical Chemistry)
Section cross-reference(s): 9, 61, 64
IT **53714-56-0**, Leuprolide
RL: AMX (Analytical matrix); ANST (Analytical study)
(9-Octadecenoic acid (Z)-, monoester with 1,2,3-propanetriol

sulfatesensitive reversed-phase liquid chromatog. determination of fluoride in)

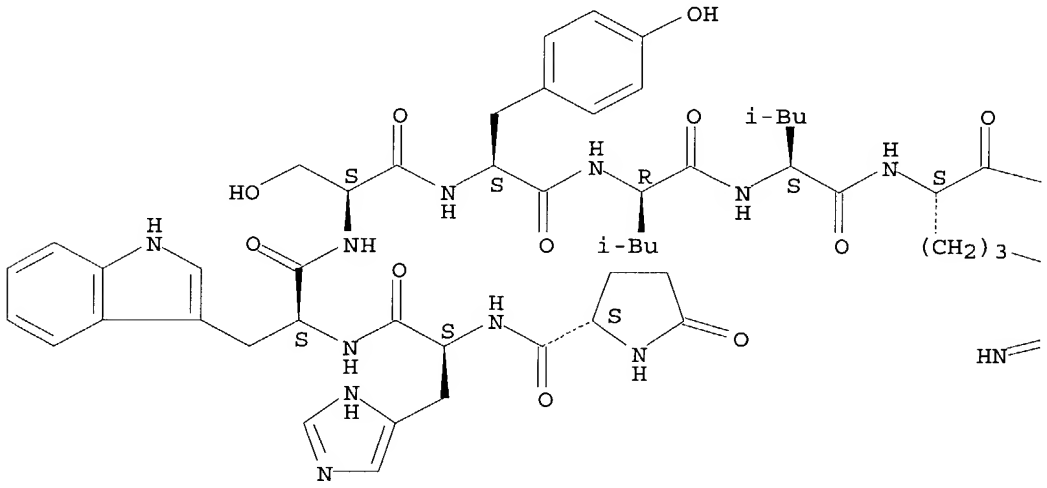
IT **53714-56-0**, Leuprolide
RL: AMX (Analytical matrix); ANST (Analytical study)
(9-Octadecenoic acid (Z)-, monoester with 1,2,3-propanetriol
sulfatesensitive reversed-phase liquid chromatog. determination of fluoride in)

RN 53714-56-0 CAPLUS

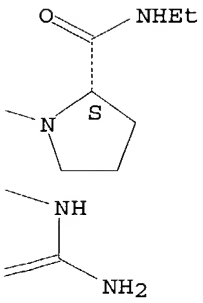
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 19 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:377184 CAPLUS
DOCUMENT NUMBER: 129:145003
TITLE: Normal outcome following administration of gonadotropin-releasing hormone (GnRH) agonist during early pregnancy
AUTHOR(S): Uehara, Shigeki; Sakahira, Hiroshi; Tamura, Mitsutoshi; Watanabe, Takanori; Yajima, Akira
CORPORATE SOURCE: Department Obstetrics Gynecology, Tohoku University School Medicine, Sendai, 980-8574, Japan
SOURCE: Congenital Anomalies (1998), 38(1), 81-85
CODEN: CGANE7; ISSN: 0914-3505
PUBLISHER: Nippon Senten Ijo Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors observed an unusual case of a woman who had received a gonadotropin-releasing hormone (GnRH) agonist (GnRH-a), leuprolide acetate, during the first trimester and early in the second trimester of pregnancy. Nevertheless, the pregnancy was uncomplicated and a healthy male infant (2670 g) was born after spontaneous labor at the 38th week of gestation. The infant suffered no malformations or respiratory complication and he achieved normal growth. Although GnRH-a is known to induce pregnancy loss, the drug does not appear to be teratogenic. Accordingly, a pregnancy that occurs during GnRH-a therapy and progresses normally should not be terminated for fear of its teratogenic effects.

CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 4

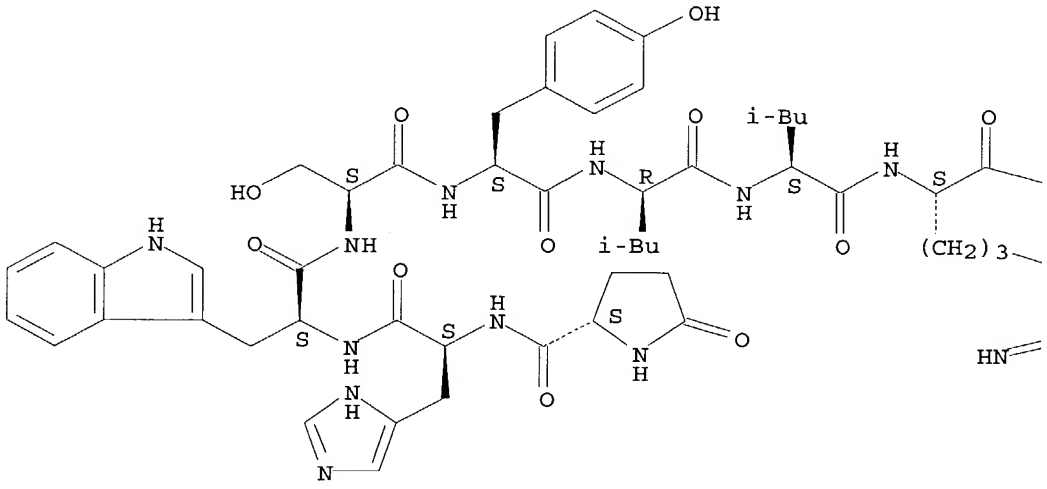
IT **53714-56-0**, Leuprolide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(normal outcome following administration of LH-RH agonist during early pregnancy)

IT **53714-56-0**, Leuprolide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(normal outcome following administration of LH-RH agonist during early pregnancy)

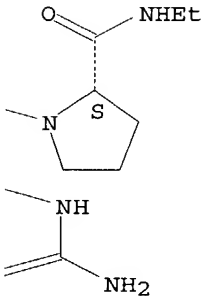
RN 53714-56-0 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 20 OF 312 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:365611 CAPLUS
DOCUMENT NUMBER: 129:48989
TITLE: GHRH Agonist. Hormone-suppressive effects of monthly microcapsule-depot form of GHRH agonist, leuprorelin
AUTHOR(S): Sudo, Katsuichi; Ogawa, Yasuaki
CORPORATE SOURCE: Pharm. Res. Div., Takeda Chem. Ind., Ltd., Japan
SOURCE: Cell (Tokyo) (1998), 30(4), 146-149
CODEN: SAIBD8; ISSN: 0386-4766
PUBLISHER: Nyu Saiensusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review, with 16 refs., of the design, pharmacokinetics and

hormone-suppressive effects of monthly microcapsule-depot form of GHRH agonist, leuprorelin, e.g. for treatment of endometriosis.

CC 1-0 (Pharmacology)
Section cross-reference(s): 2, 63

IT **53714-56-0**, Leuprorelin
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(GHRH Agonist. Hormone-suppressive effects of monthly microcapsule-depot form of GHRH agonist, leuprorelin)

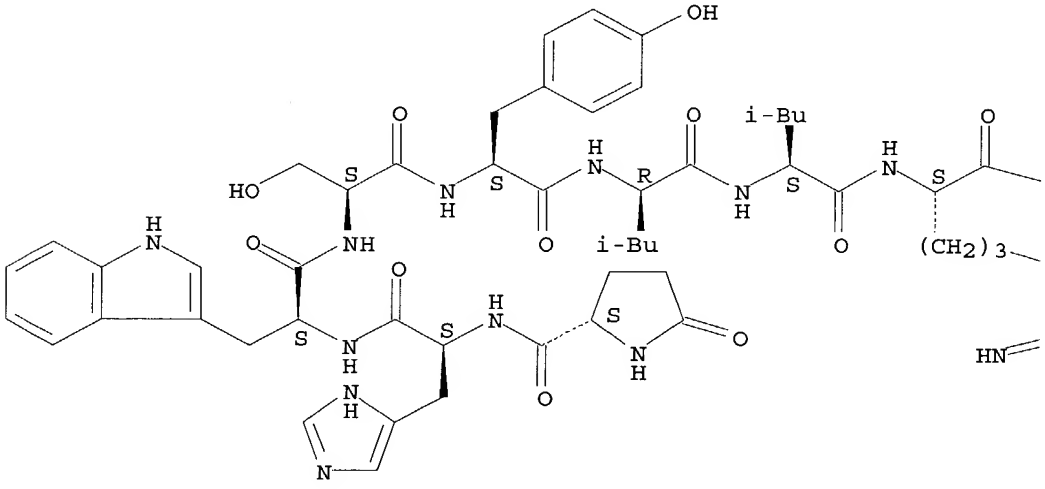
IT **53714-56-0**, Leuprorelin
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(GHRH Agonist. Hormone-suppressive effects of monthly microcapsule-depot form of GHRH agonist, leuprorelin)

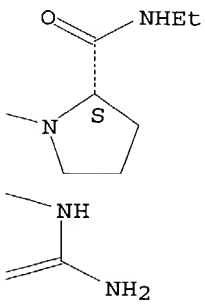
RN 53714-56-0 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A





L15 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:248014 CAPLUS
DOCUMENT NUMBER: 139:7345
TITLE: Peptides Form Stereoselective Complexes with Chiral Polymers
AUTHOR(S): Slager, Joram; Cohen, Yachin; Khalfin, Rafail; Talmon, Yeshayahu; Domb, Abraham J.
CORPORATE SOURCE: Department of Medicinal Chemistry and Natural Products School of Pharmacy, Hebrew University, Jerusalem, 91120, Israel
SOURCE: Macromolecules (2003), 36(9), 2999-3000
CODEN: MAMOBX; ISSN: 0024-9297
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have discovered reversible stereoselective complexes between L-peptides and enantioselective D-polyesters. The spontaneously formed complexes obtained as uniform microparticles of 2-5 μm in size showed controlled release of the interlocked peptides. The stereoselective complexation occurred only with poly(D-lactic acid), not with poly(L-lactic acid) or racemic poly(DL-lactic acid) as shown by SAXS studies.

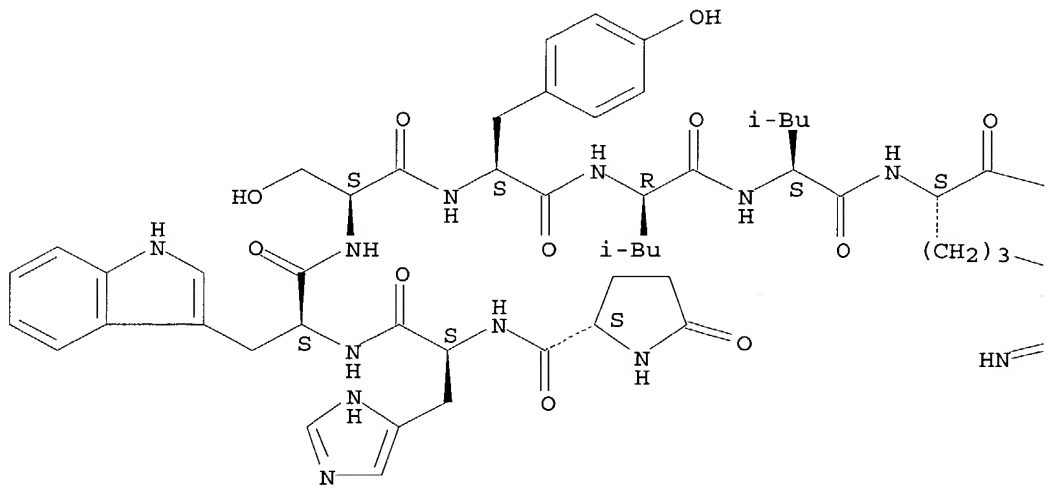
CC 35-8 (Chemistry of Synthetic High Polymers)
IT **532959-43-6P 532959-44-7P** 532959-45-8P 532959-46-9P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(peptides form stereoselective complexes with poly(D-lactic acid))
IT **532959-43-6P 532959-44-7P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(peptides form stereoselective complexes with poly(D-lactic acid))
RN 532959-43-6 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, compd. with (2R)-2-hydroxypropanoic acid homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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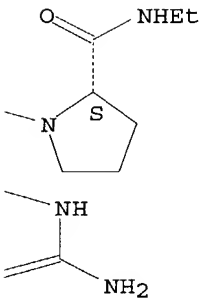

CM 2

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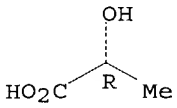
CMF (C3 H6 O3)x
CCI PMS

CM 3

CRN 10326-41-7
CMF C3 H6 O3

Absolute stereochemistry.



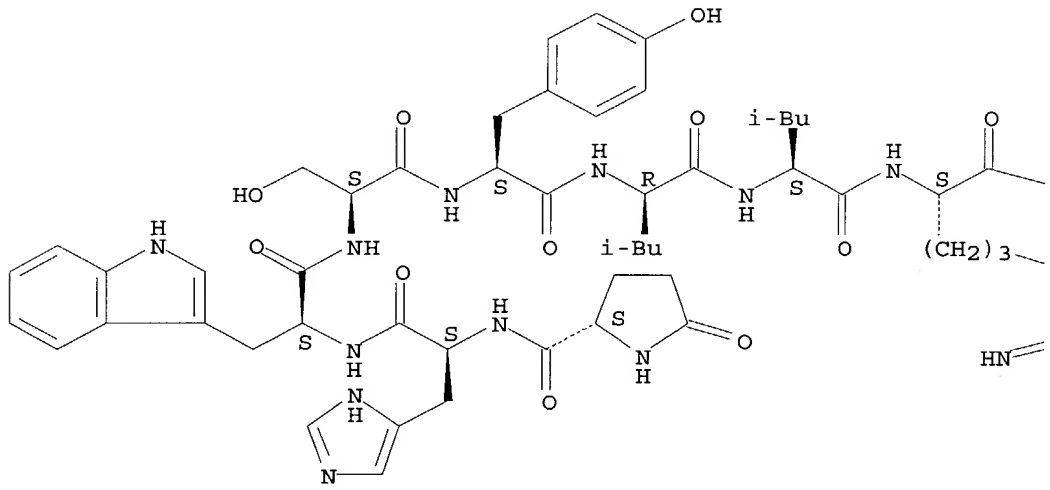
RN 532959-44-7 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, compd. with poly[oxy[(1R)-1-methyl-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)

CM 1

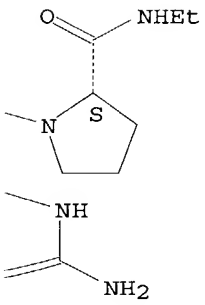
CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A

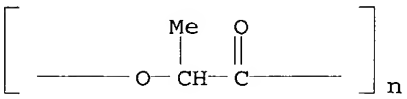


PAGE 1-B



CM 2

CRN 26917-25-9
CMF (C3 H4 O2)n
CCI PMS



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:24249 CAPLUS
DOCUMENT NUMBER: 139:185509
TITLE: In vitro transdermal iontophoretic delivery of leuprolide-mechanisms under constant voltage application
AUTHOR(S): Kochhar, Charu; Imanidis, Georgios
CORPORATE SOURCE: Institute of Pharmaceutical Technology, University of Basel, Basel, 4056, Switz.
SOURCE: Journal of Pharmaceutical Sciences (2003), 92(1), 84-96
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The transdermal iontophoretic delivery of Leuprolide, a nonapeptide LHRH agonist was studied with the aim of understanding the mechanisms of iontophoresis. Permeation studies were carried out at pH 4.5 and 7.2, at which the average ionic valence of the drug mol. was roughly 2 and 1, resp. Heat-separated human epidermal membrane was subjected to constant voltage within the range of 250 to 1000 mV during the iontophoretic phase. Iontophoretic enhancement at pH 7.2 was greated than at 4.5. A model for iontophoretic enhancement was developed that takes into consideration the membrane alterations caused by iontophoresis depicted as increased porosity and the permeation through lipid pathways of the stratum corneum. Model-based evaluation yielded that first, the porosity increased with the applied voltage to as much as three times the original at 1000 mV. Second, the lipid pathways contributed approx. 20% to the total permeation during the passive phase. Third, the electro-osmotic flow contributed significantly to the enhancement and its direction was from anode to cathode at pH 7.2 and the opposite at pH 4.5. The magnitude of the electro-osmotic flow was at pH 4.5 somewhat lower than at pH 7.2. Addition of a neg. charged water soluble peptide, Acetyl leucine leucinolyl phosphate as an adjuvant led to twofold increase in the enhancement factor at pH 4.5 and a decrease in the magnitude of the electro-osmotic flow from cathode to anode. Repeated iontophoretic applications of 250 mV on the same skin specimen resulted in same enhancement every time and did not cause any barrier alterations when applied for 1 h every 24 h, which was not the case if the duration between the two iontophoretic applications was only 3 h.

CC 63-6 (Pharmaceuticals)
IT **581088-28-0**

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transdermal iontophoretic delivery of leuprolide-mechanisms under constant voltage application)

IT **581088-28-0**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transdermal iontophoretic delivery of leuprolide-mechanisms under constant voltage application)

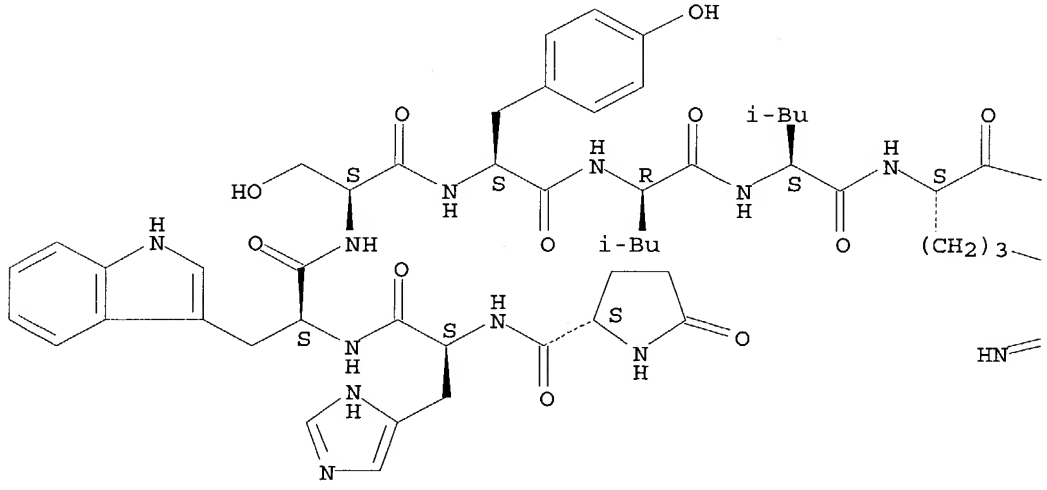
RN 581088-28-0 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, diacetate (salt) (9CI) (CA INDEX NAME)

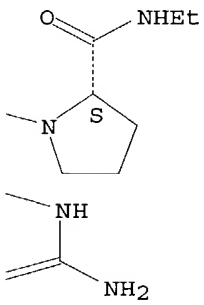
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

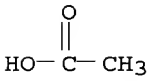
PAGE 1-A





CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:849464 CAPLUS
DOCUMENT NUMBER: 137:358129
TITLE: Preventives for postoperative recurrence of premenopausal breast cancer
INVENTOR(S): Igari, Yasutaka; Kusaka, Masami
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002087616	A1	20021107	WO 2002-JP4071	20020424

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2003012552 A2 20030115 JP 2002-122734 20020424
EP 1382350 A1 20040121 EP 2002-722741 20020424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: JP 2001-128032 A 20010425
WO 2002-JP4071 W 20020424
OTHER SOURCE(S): MARPAT 137:358129

AB Disclosed are remedies for postoperative recurrence of premenopausal breast cancer containing a GnRH agonist or antagonist which makes it possible to prevent the postoperative recurrence of premenopausal breast cancer without showing any serious side effects. By using sustained-release microcapsules, the drug effect can be sustained over a long time without frequently administering the drug. Thus, the postoperative recurrence of premenopausal breast cancer can be conveniently prevented over a prolonged period of time. Clin. studies showed that s.c. administration of Lupron Depot was effective to prevent recurrence of the breast cancer.

IC ICM A61K045-00
ICS A61K038-09; A61K009-50; A61K009-52; A61K047-34; A61P005-08; A61P035-00; A61P043-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

IT 53714-56-0 **474787-24-1**, Leuprolide hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH agonists or antagonists as preventives for postoperative recurrence of premenopausal breast cancer)

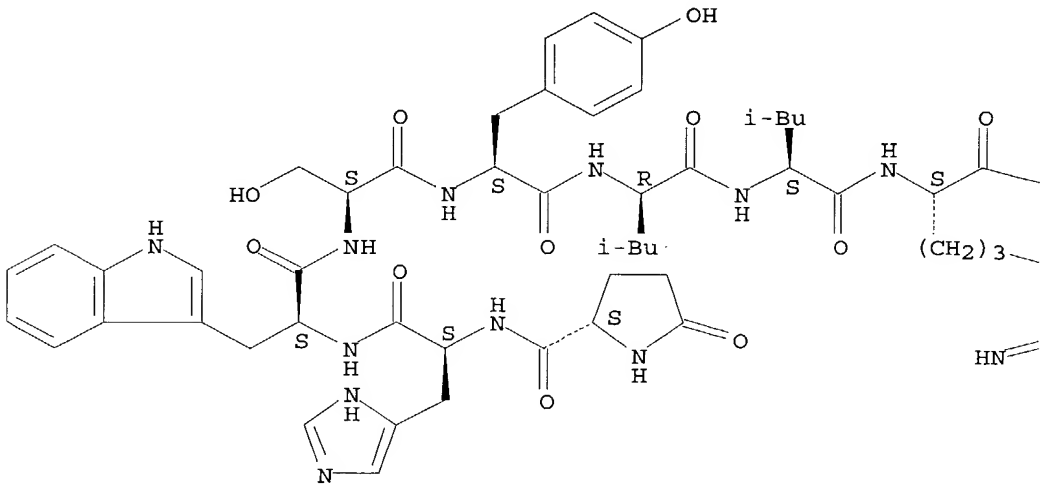
IT **474787-24-1**, Leuprolide hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH agonists or antagonists as preventives for postoperative recurrence of premenopausal breast cancer)

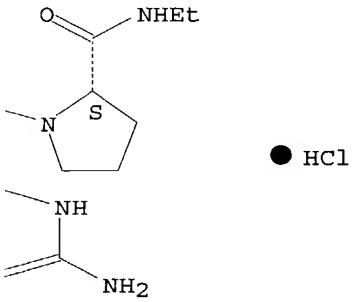
RN 474787-24-1 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A





REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:602626 CAPLUS
DOCUMENT NUMBER: 134:9231
TITLE: Hydrophobic ion pair formation between leuprolide and sodium oleate for sustained release from biodegradable polymeric microspheres
AUTHOR(S): Choi, S. H.; Park, T. G.
CORPORATE SOURCE: Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Taejon, 305-701, S. Korea
SOURCE: International Journal of Pharmaceutics (2000), 203(1-2), 193-202
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leuprolide acetate, an analog of LH-releasing hormone (LH-RH), was hydrophobically ion paired with a long chain fatty acid, sodium oleate, in an aqueous solution Solution behaviors of the complex formed between leuprolide and sodium oleate were investigated in terms of aqueous solubility, turbidity, particle size, and zeta potential as a function of molar ratio between the two species. It was found that with increasing the stoichiometric molar amts. of sodium oleate to leuprolide approached up to 2.5-3, the solution became gradually turbid with increasing particle sizes, indicating leuprolide precipitation as a result of hydrophobic ion pairing. On the other hand, beyond that critical molar ratio range, the solution turned into clear with much reduced particle size, indicative of micelle formation. The hydrophobically modified leuprolide-oleate complex was lyophilized and directly encapsulated within biodegradable poly(d,l-lactic-co-glycolic acid) (PLGA) microspheres via a single oil-in-water (O/W) emulsion method. Microsphere morphol., leuprolide release behavior, and polymer mass erosion profiles were examined in comparison to the PLGA microspheres prepared with free leuprolide.

CC 63-5 (Pharmaceuticals)

IT **308811-89-4P**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(hydrophobic ion pair formation between leuprolide and sodium oleate for sustained release from biodegradable polymeric microspheres)

IT **308811-89-4P**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(hydrophobic ion pair formation between leuprolide and sodium oleate for sustained release from biodegradable polymeric microspheres)

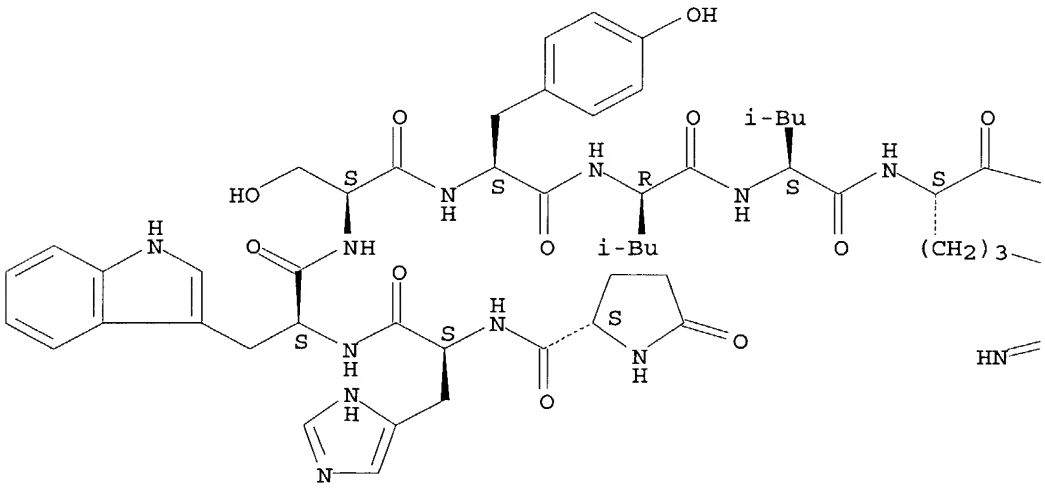
RN 308811-89-4 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, (9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

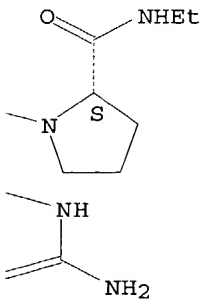
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A

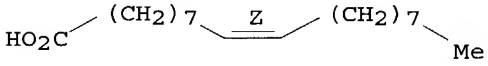




CM 2

CRN 112-80-1
CMF C18 H34 O2

Double bond geometry as shown.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:468574 CAPLUS
DOCUMENT NUMBER: 131:106841
TITLE: Sustained release compositions, process for producing the same and utilization thereof
INVENTOR(S): Saikawa, Akira; Igari, Yasutaka; Hata, Yoshio; Yamamoto, Kazumichio
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9936099	A1	19990722	WO 1999-JP86	19990113

W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2316273	AA	19990722	CA 1999-2316273	19990113	
AU 9918897	A1	19990802	AU 1999-18897	19990113	
AU 758596	B2	20030327			
EP 1048301	A1	20001102	EP 1999-900300	19990113	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
BR 9906903	A	20001212	BR 1999-6903	19990113	
TR 200002059	T2	20010122	TR 2000-20000205	19990113	
NZ 505651	A	20030829	NZ 1999-505651	19990113	
JP 11269094	A2	19991005	JP 1999-7566	19990114	
US 6740634	B1	20040525	US 2000-582926	20000706	
NO 2000003530	A	20000914	NO 2000-3530	20000707	
HR 2000000471	A1	20001231	HR 2000-471	20000713	
PRIORITY APPLN. INFO.:			JP 1998-6412	A 19980116	
			WO 1999-JP86	W 19990113	

OTHER SOURCE(S): MARPAT 131:106841

AB The invention relates to sustained release compns. containing a physiol. active substance [peptide A] or its salt, hydroxynaphthoic acid or its salt and a biodegradable polymer or its salt; and drugs, etc. containing these compns.

IC ICM A61K047-30
ICS A61K047-12; A61K037-02

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2

IT 92-70-6, 3-Hydroxy-2-naphthoic acid 9034-40-6, Lh-rh 26100-51-6, DL-Lactic acid polymer 30440-92-7, Hydroxynaphthoic acid 34346-01-5, Glycolic acid-lactic acid copolymer **88793-81-1** 168395-24-2 230638-75-2
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(sustained release compns., process for producing the same and utilization thereof)

IT **88793-81-1**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(sustained release compns., process for producing the same and utilization thereof)

RN 88793-81-1 CAPLUS

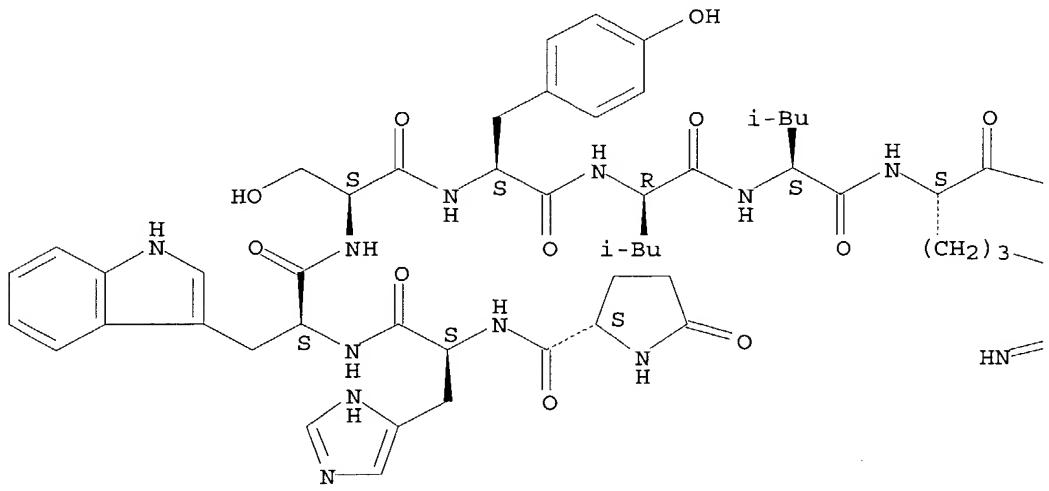
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

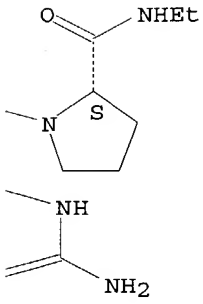
CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A

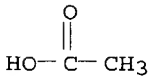


PAGE 1-B



CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:823425 CAPLUS
DOCUMENT NUMBER: 123:266128
TITLE: Formulations and method of the percutaneous administration of leuprolide
INVENTOR(S): Lu, Mou-Ying Fu; Subba, Rao Gowdahallin N.; Lee, Dennis Y.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5446025	A	19950829	US 1992-897680	19920612

PRIORITY APPLN. INFO.: US 1992-897680 19920612

AB Compns. useful for the percutaneous administration of leuprolide comprise 1-100 mg/mL of leuprolide in its free base form, a cutaneous membrane penetration enhancing component, and a pharmaceutically acceptable carrier. The cutaneous membrane transport enhancing component comprises 1-15% urea, 1-5% menthol, 0.5-5% Me salicylate, and 0.5-5% camphor. Thus, a gel contained menthol 100, camphor 100, leuprolide 100 and hydroxypropyl cellulose 200 mg, 200 μL me salicylate and 8 mL EtOH.

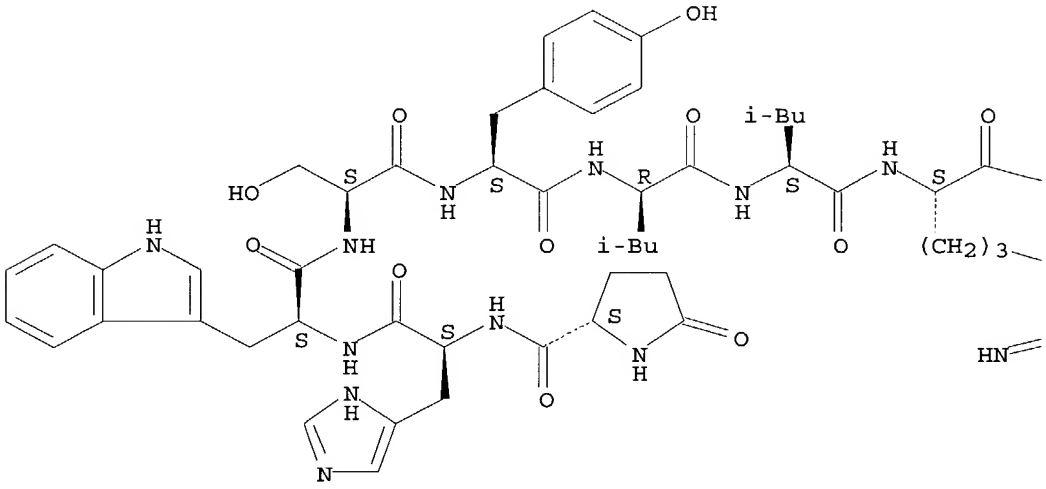
IC ICM A61K037-00
ICS A61K037-02; C07K005-00; C07K007-00
NCL 514015000
CC 63-6 (Pharmaceuticals)
IT 57-13-6, Urea, biological studies 76-22-2, Camphor. 119-36-8, Methyl salicylate 1490-04-6, Menthol 53714-56-0, Leuprolide 74381-53-6, Leuprolide acetate **148335-51-7 169047-57-8**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulations for percutaneous administration of leuprolide)
IT **148335-51-7 169047-57-8**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulations for percutaneous administration of leuprolide)
RN 148335-51-7 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, mono-1-decanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

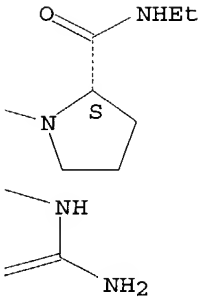
CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



CM 2

CRN 20283-21-0
CMF C10 H22 O3 S

$HO_3S-(CH_2)_9-Me$

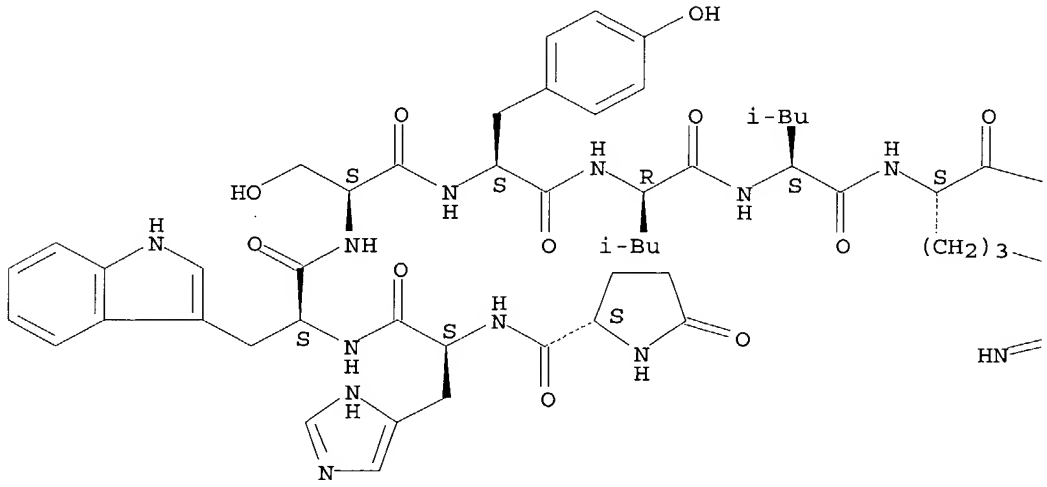
RN 169047-57-8 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, monohexadecanoate (salt) (9CI) (CA INDEX NAME)

CM 1

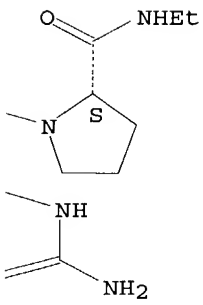
CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



CM 2

CRN 57-10-3
CMF C16 H32 O2

$HO_2C-(CH_2)_{14}-Me$

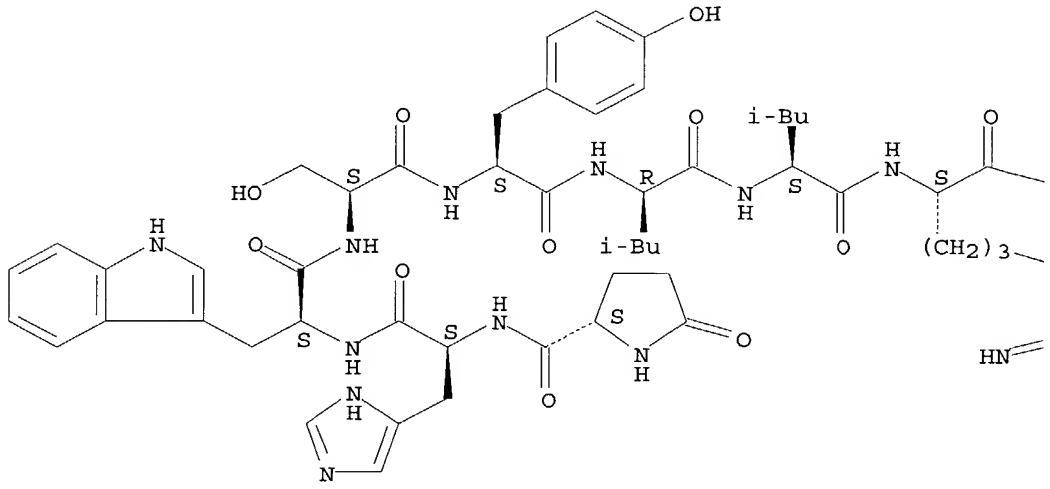
L15 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:491446 CAPLUS
DOCUMENT NUMBER: 121:91446
TITLE: Effect of formulation adjuvants on gastrointestinal absorption of leuprolide acetate
AUTHOR(S): Adjei, A.; Love, S.; Johnson, E.; Diaz, G.; Greer, J.; Haviv, F.; Bush, E.
CORPORATE SOURCE: Pharm. Prod. Div., Abbott Lab., North Chicago, IL, 60064-2204, USA
SOURCE: Journal of Drug Targeting (1993), 1(3), 251-8
CODEN: JDTAEH; ISSN: 1061-186X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Leuprolide acetate, [D-Leu6-desGly10]LH-RH ethylamide, a highly potent superagonist of LH-releasing hormone (LH-RH), was administered by intraduodenal (ID) injection to male castrate rats in a saline solution Absorption was low, approx. 0.01% and 0.08% by oral and ID administration resp., compared with i.v. controls. An aqueous formulation and a water in oil emulsion of a lipophilic salt, a decane sulfonic acid derivative of [D-Leu6-desGly10]LH-RH ethylamide gave ID bioavailabilities of approx. 0.2% and 1%, resp. Evaluation of formulation effects on the oral absorption of leuprolide showed that lipophilicity, surfactant and vehicle properties significantly affected ID absorption of leuprolide. Absolute bioavailability of the drug in typical emulsion systems ranged from approx. 3 to 10% and represent an improvement of about 100 fold in gastrointestinal bioavailability of this peptide. The implications of these findings relative to the effect of formula adjuvants on oral absorption of leuprolide and other peptides following ID administration are discussed.
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1
IT 74381-53-6, Leuprolide acetate **148335-51-7**
RL: BIOL (Biological study)
(absorption of, by digestive tract, formulation adjuvants effect on)
IT **148335-51-7**
RL: BIOL (Biological study)
(absorption of, by digestive tract, formulation adjuvants effect on)
RN 148335-51-7 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, mono-1-decanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

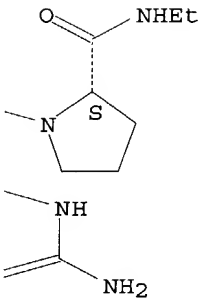
CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



CM 2

CRN 20283-21-0
CMF C10 H22 O3 S

$HO_3S-(CH_2)_9-Me$

L15 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:200425 CAPLUS
DOCUMENT NUMBER: 120:200425
TITLE: Extended-release pharmaceuticals containing salts of peptides with carboxy-terminated polyesters

INVENTOR(S): Hutchinson, Francis Gowland
PATENT ASSIGNEE(S): Zeneca Ltd., UK
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9324150	A1	19931209	WO 1993-GB1079	19930525
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA				
RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9303358	A	19940915	ZA 1993-3358	19930513
IL 105710	A1	20010319	IL 1993-105710	19930516
AU 9340847	A1	19931230	AU 1993-40847	19930525
AU 682310	B2	19971002		
GB 2282066	A1	19950329	GB 1994-23366	19930525
GB 2282066	B2	19961106		
NL 9320034	A	19950403	NL 1993-20034	19930525
NL 195056	C	20030701		
HU 70177	A2	19950928	HU 1994-3371	19930525
DE 4392401	T	19970724	DE 1993-4392401	19930525
ES 2107357	A1	19971116	ES 1994-50004	19930525
ES 2107357	B1	19981016		
CH 688911	A	19980529	CH 1993-311	19930525
SK 280320	B6	19991108	SK 1994-1434	19930525
RU 2152225	C1	20000710	RU 1994-46097	19930525
CH 690491	A	20000929	CH 1993-68098	19930525
AT 9309019	A	20001015	AT 1993-9019	19930525
AT 407702	B	20010525		
CZ 292449	B6	20030917	CZ 1994-2937	19930525
FR 2691631	A1	19931203	FR 1993-6432	19930528
FR 2691631	B1	19950609		
BE 1006143	A3	19940524	BE 1993-551	19930528
FI 9405553	A	19950125	FI 1994-5553	19941125
NO 9404535	A	19950125	NO 1994-4535	19941125
DK 9401353	A	19941128	DK 1994-1353	19941128
SE 9404115	A	19941128	SE 1994-4115	19941128
SE 501970	C2	19950703		
US 5889110	A	19990330	US 1995-473303	19950607
US 6034175	A	20000307	US 1999-235270	19990122
US 2002198315	A1	20021226	US 2001-988068	20011116

PRIORITY APPLN. INFO.:

GB 1992-11268	A	19920528
US 1993-65771	B3	19930524
WO 1993-GB1079	A	19930525
US 1995-473303	A1	19950607
US 1998-161707	B1	19980929

AB Novel salts composed of a cation derived from a peptide containing ≥1 one basic group and an anion derived from a carboxy-terminated polyester are used for manufacture of extended-release pharmaceutical compns. Goserelin acetate (I) and D,L-lactide-glycolide copolymer (II) were disolved in glacial acetic acid and the solution was added dropwise to liquid N and the frozen droplets were freeze-dried under vacuum for 24h, then dried at 50° for 24 h under vacuum to give I.II salts (III) containing 25% I. The dried III was dissolved in CH2Cl2 and was cast as a film of 0.02μm thickness. The release of goserelin from the film, when incubated in phosphate buffered saline at pH=7.4 and 37°, continued for >2 wk

and by third wk the film had virtually degraded completely and disappeared from the buffer.

IC ICM A61K047-48
ICS A61K009-20; A61K009-16

CC 63-5 (Pharmaceuticals)

IT 50-56-6D, Oxytocin, salts with carboxy-terminated polyesters 56-87-1D, Lysine, polymers with neutral amino acids, salts with carboxy-terminated polyesters 58-82-2D, Bradykinin, salts with carboxy-terminated polyesters 74-79-3D, Arginine, polymers with neutral amino acids, salts with carboxy-terminated polyesters 1393-25-5D, Secretin, salts with carboxy-terminated polyesters 1405-97-6D, Gramicidin, salts with carboxy-terminated polyesters 1947-37-1D, Tetragastrin, salts with carboxy-terminated polyesters 5534-95-2D, Pentagastrin, salts with carboxy-terminated polyesters 8011-61-8D, Tyrocidine, salts with carboxy-terminated polyesters 9001-01-8D, Kallikrein, salts with carboxy-terminated polyesters 9001-25-6D, Blood coagulation factor VII, salts with carboxy-terminated polyesters 9001-28-9D, Blood coagulation factor IX, salts with carboxy-terminated polyesters 9002-60-2D, Adrenocorticotrophic hormone, salts with carboxy-terminated polyesters 9002-61-3D, Chorionic gonadotrophin, human, salts with carboxy-terminated polyesters 9002-62-4D, Prolactin, salts with carboxy-terminated polyesters 9002-64-6D, Parathyroid hormone, salts with carboxy-terminated polyesters 9002-67-9D, Luteinizing hormone, salts with carboxy-terminated polyesters 9002-68-0D, FSH, salts with carboxy-terminated polyesters 9002-71-5D, Thyroid stimulating hormone, salts with carboxy-terminated polyesters 9002-76-0D, Gastrin, salts with carboxy-terminated polyesters 9002-79-3D, Melanotropin, salts with carboxy-terminated polyesters 9004-10-8D, Insulin, salts with carboxy-terminated polyesters 9007-12-9D, Calcitonin, salts with carboxy-terminated polyesters 9007-92-5D, Glucagon, salts with carboxy-terminated polyesters 9011-97-6D, Cholecystokinin, salts with carboxy-terminated polyesters 9015-94-5D, Renin, salts with carboxy-terminated polyesters 9034-39-3D, Growth hormone releasing factor, salts with carboxy-terminated polyesters 9034-40-6D, Luteinizing hormone releasing hormone, salts with carboxy-terminated polyesters 9039-53-6D, Urokinase, salts with carboxy-terminated polyesters 9061-61-4D, Nerve growth factor, salts with carboxy-terminated polyesters 9063-57-4D, Taftsin, salts with carboxy-terminated polyesters 9066-59-5D, Lysozyme chloride, salts with carboxy-terminated polyesters 11000-17-2D, Vasopressin, salts with carboxy-terminated polyesters 11085-36-2D, Human placental lactogen, salts with carboxy-terminated polyesters 11128-99-7D, Angiotensin II, salts with carboxy-terminated polyesters 17650-98-5D, Cerulein, salts with carboxy-terminated polyesters 24305-27-9D, salts with carboxy-terminated polyesters 24937-47-1D, Polyarginine, salts with carboxy-terminated polyesters 25104-18-1D, Polylysine, salts with carboxy-terminated polyesters 25212-18-4D, Polyarginine, salts with carboxy-terminated polyesters 31014-78-5D, salts with carboxy-terminated polyesters 31362-50-2D, Bombesin, salts with carboxy-terminated polyesters 33507-63-0D, Substance p, analogs and antagonists, salts with carboxy-terminated polyesters 37221-79-7D, Vasoactive intestinal peptide, salts with carboxy-terminated polyesters 38000-06-5D, Polylysine, salts with carboxy-terminated polyesters 38234-21-8D, salts with carboxy-terminated polyesters 39379-15-2D, Neurotensin, salts with carboxy-terminated polyesters 51110-01-1D, Somatostatin, salts with carboxy-terminated polyesters 52906-92-0D, Motilin, salts with carboxy-terminated polyesters 53714-56-0D, salts with carboxy-terminated polyesters 57773-63-4D, salts with carboxy-terminated polyesters 57773-65-6D, salts with carboxy-terminated polyesters 57982-77-1D, salts with carboxy-terminated polyesters 59392-49-3D, Gastric inhibitory peptide,

salts with carboxy-terminated polyesters 60118-07-2D, Endorphins, salts with carboxy-terminated polyesters 60529-76-2D, Thymopoietin, salts with carboxy-terminated polyesters 61512-21-8D, Thymosin, salts with carboxy-terminated polyesters 62229-50-9D, Epidermal growth factor, salts with carboxy-terminated polyesters 62683-29-8D, Colony stimulating factor, salts with carboxy-terminated polyesters 63340-72-7D, Thymus humoral factor, salts with carboxy-terminated polyesters 63958-90-7D, Serum thymic factor, salts with carboxy-terminated polyesters 65807-02-5D, salts with carboxy-terminated polyesters 66866-63-5D, salts with carboxy-terminated polyesters 70904-56-2D, Kyotorphin, salts with carboxy-terminated polyesters 74913-18-1D, Dynorphin, salts with carboxy-terminated polyesters 76932-56-4D, salts with carboxy-terminated polyesters 153603-64-6 153603-65-7 153603-66-8 153603-67-9 **153724-53-9 153825-04-8**
RL: BIOL (Biological study)
(extended-release pharmaceuticals containing)

IT **153724-53-9 153825-04-8**
RL: BIOL (Biological study)
(extended-release pharmaceuticals containing)

RN 153724-53-9 CAPLUS

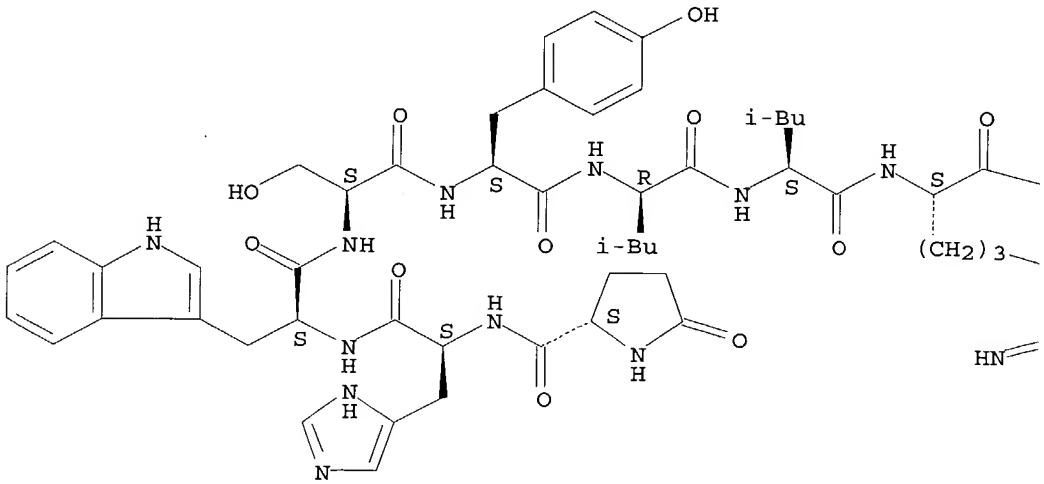
CN Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, compd. with 3,6-dimethyl-1,4-dioxane-2,5-dione polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

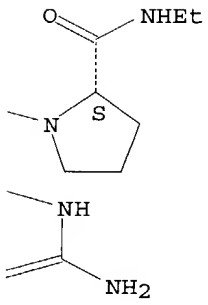
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



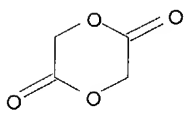


CM 2

CRN 26780-50-7
CMF (C6 H8 O4 . C4 H4 O4)x
CCI PMS

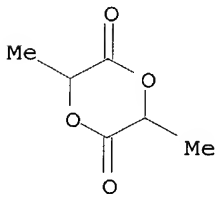
CM 3

CRN 502-97-6
CMF C4 H4 O4



CM 4

CRN 95-96-5
CMF C6 H8 O4



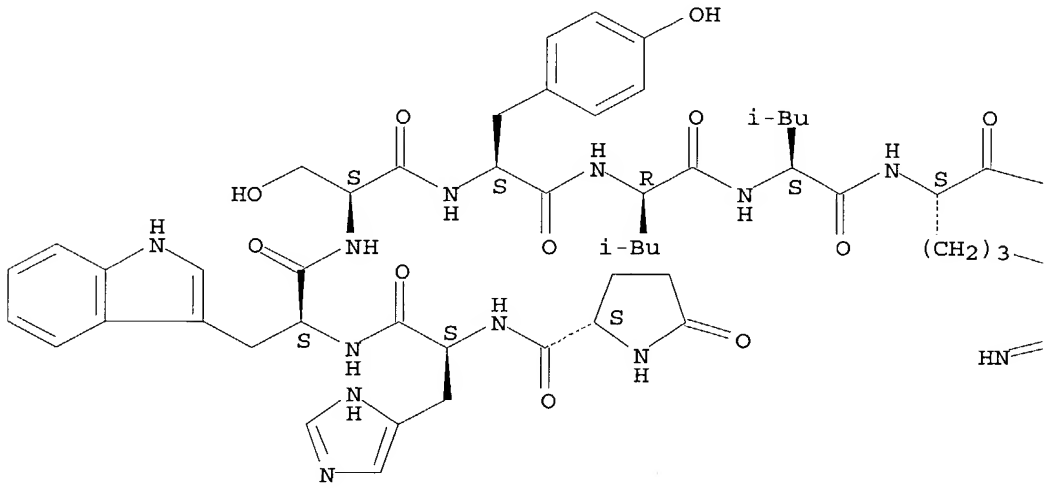
RN 153825-04-8 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, compd. with hydroxyoctadecanoic acid homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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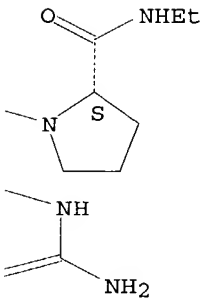


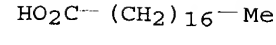
CM 2

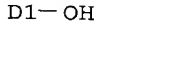
CRN 72006-34-9
CMF (C18 H36 O3)x
CCI PMS

CM 3

CRN 1330-70-7

CMF C18 H36 O3
CCI IDS





L15 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:434201 CAPLUS
DOCUMENT NUMBER: 119:34201
TITLE: Effect of ion-pairing on 1-octanol-water partitioning of peptide drugs. I: The nonapeptide leuprolide acetate
AUTHOR(S): Adjei, A.; Rao, S.; Garren, J.; Menon, G.; Vadnere, M.
CORPORATE SOURCE: Pharm. Prod., Abbott Lab., North-Chicago, IL, 60064, USA
SOURCE: International Journal of Pharmaceutics (1993), 90(2), 141-9
CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leuprolide acetate is a nonapeptide with virtually no lipid solubility It has multiple ionizable sites and exists in an ionized form across a wide pH range of physiol. interest. Studies were conducted to determine the effect of counterions on the distribution of leuprolide into octanol. Counterions from the following acids were investigated: alkylsulfonic acids (C = 1, 4, 6, 8, 10), salicylate acid, and dehydrocholic acid. The distribution behavior was studied as a function of pH and counterion concentration Results showed that methane- and butanesulfonate do not help partitioning of leuprolide into the octanol phase although there is a slight improvement in lipophilicity of the drug with increasing pH. For the C6-10 alkylsulfonates the partitioning increases significantly in the following order: hexane- <octane- <decanesulfonate. A math. model was developed to describe the complex partitioning behavior of this peptide. Data for salicylate indicated marginal effect on partitioning of leuprolide. Results obtained for dehydrocholate showed no improvement in lipophilicity of the drug suggesting that the acid is too weak (high pKa) and may be sterically hindered from forming an effective ion pair. It was observed that increase in lipophilicity of leuprolide ion pairs may be proportional to the extent of ionization of the imidazolyl nitrogen of histidine, the type of counterion, and number of lipophilic counterions per mol. Also, the lipophilicity of the ion pairs may be proportional to pKa of the acid from which the anion is derived, i.e., sulfonic acid (pKa less than 2.0) > salicylic acid (pKa = 3.0) > dehydrocholic acid (pKa greater than 6.0). For the alkylsulfonate series a plot of log K (where K represents ion pair equilibrium constant) vs. number of carbon atoms in the alkyl chain yielded a straight line with a slope of 0.5 per methylene group. This value is in good agreement with literature values of the Hansch π constant for a methylene group. Implications of these findings relative to dosage form development of leuprolide are discussed.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 2

IT **148335-51-7 148335-52-8 148335-53-9 148352-41-4**
RL: BIOL (Biological study)

(formation and partition of)

IT **148335-51-7 148335-52-8 148335-53-9 148352-41-4**
RL: BIOL (Biological study)
(formation and partition of)

RN 148335-51-7 CAPLUS

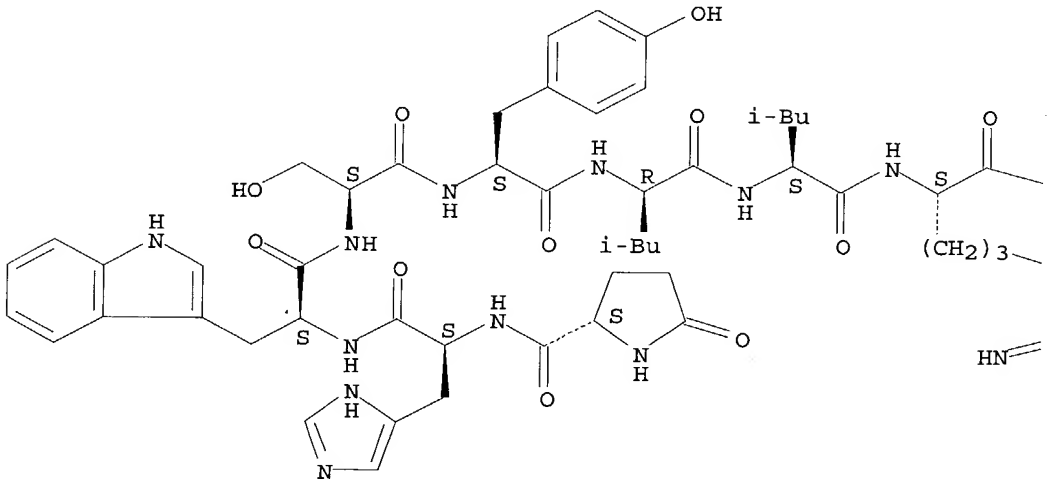
CN Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, mono-1-decanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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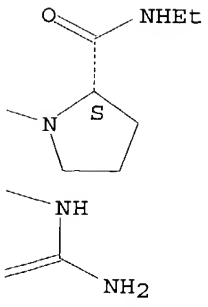


CM 2

CRN 20283-21-0
CMF C10 H22 O3 S

$HO_3S-(CH_2)_9-Me$

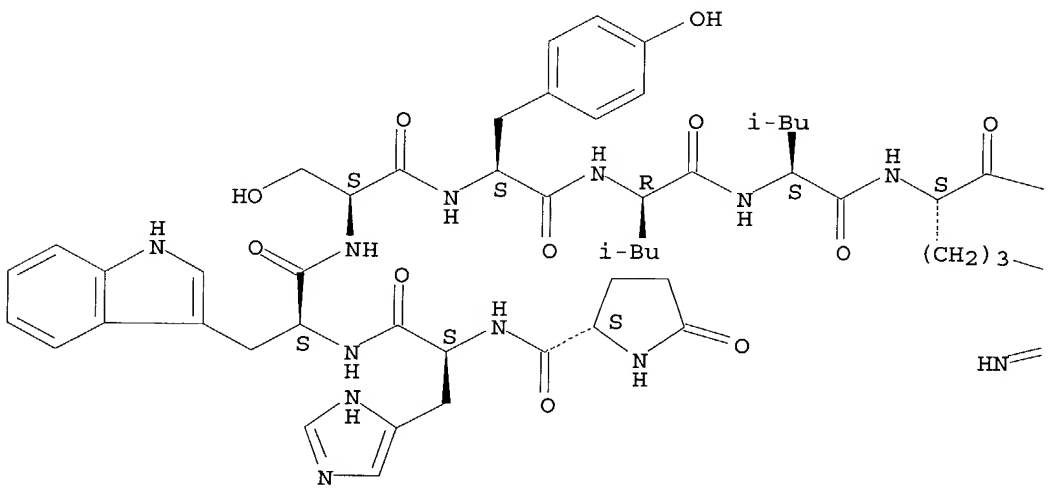
RN 148335-52-8 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, mono-1-hexanesulfonate (1:1) (salt) (9CI) (CA INDEX NAME)

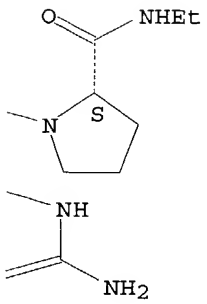
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A





CM 2

CRN 13595-73-8
CMF C6 H14 O3 S

Me— $(CH_2)_5$ — SO_3H

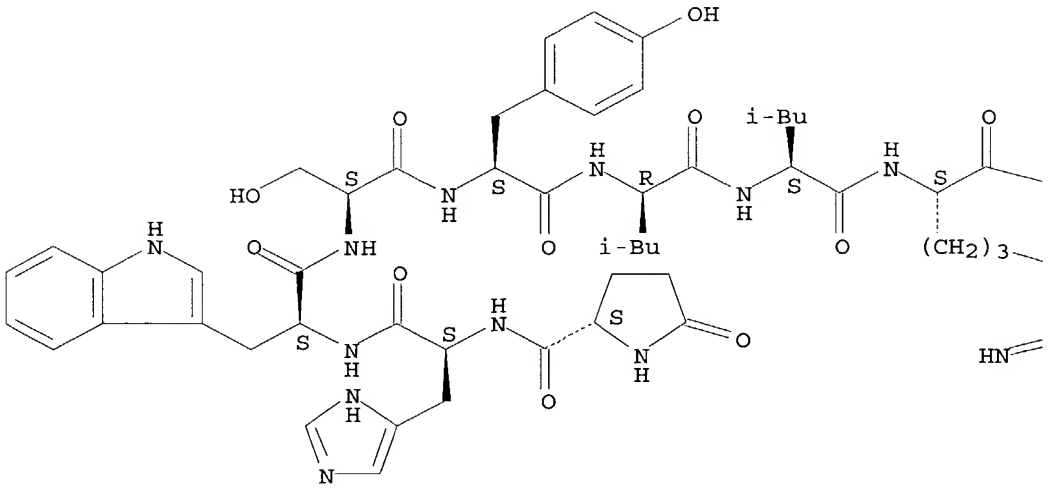
RN 148335-53-9 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide-, mono-1-butanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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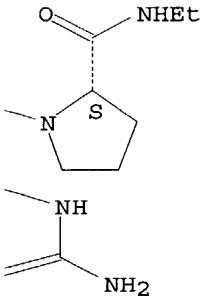
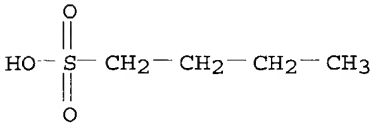


CM 2

CRN 2386-47-2
CMF C4 H10 O3 S



RN 148352-41-4 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-

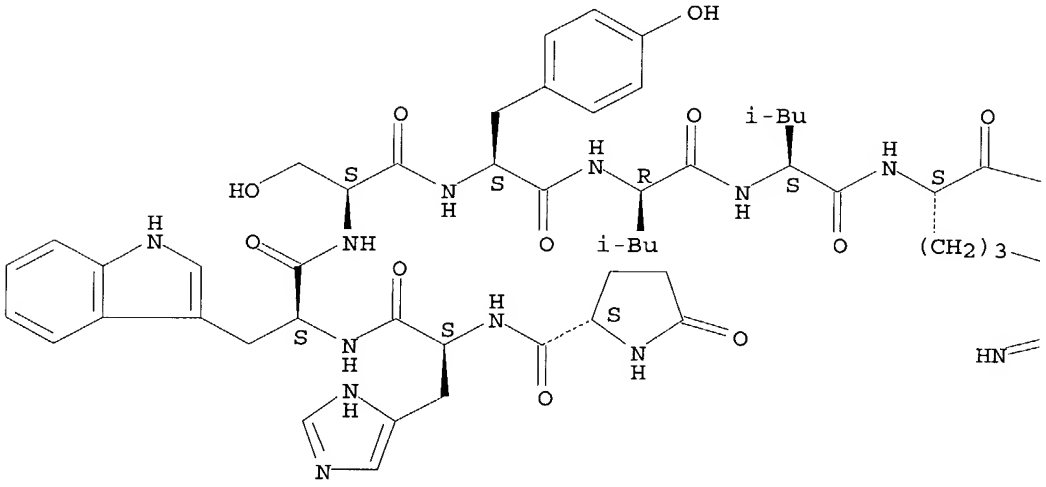
prolinamide)-10-deglycinamide-, mono-1-octanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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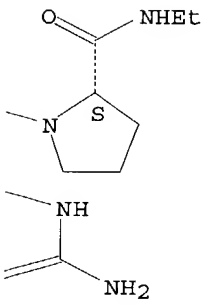


CM 2

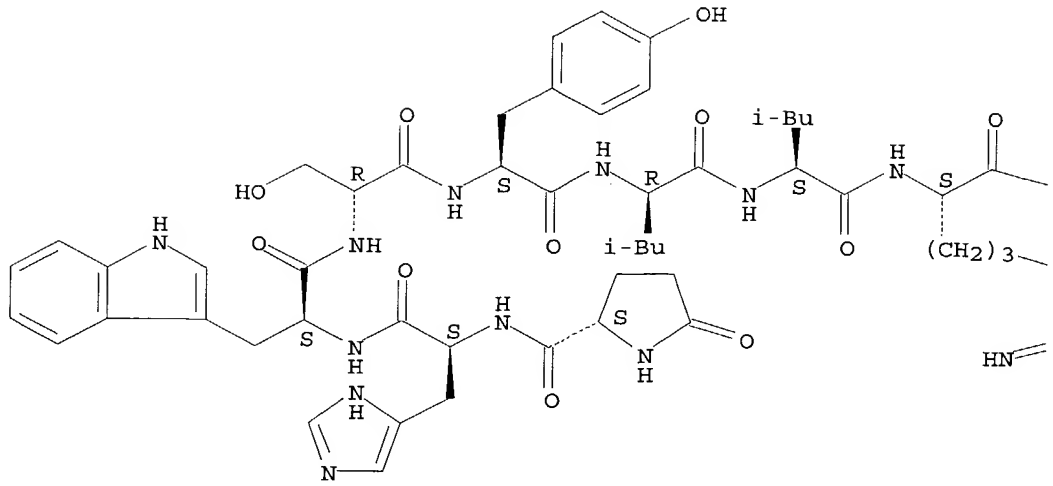
CRN 3944-72-7
CMF C8 H18 O3 S

Me— $(CH_2)_7$ — SO_3H

L15 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:813 CAPLUS
DOCUMENT NUMBER: 114:813
TITLE: Suppressive effect of TAP-144-SR, a sustained-release formulation of a potent GnRH agonist, on the reproductive function in male rats
AUTHOR(S): Maeda, Keiichiro; Fujino, Akiko; Tsukamura, Hiroko; Ohkura, Satoshi; Yokoyama, Akira
CORPORATE SOURCE: Sch. Agric., Nagoya Univ., Nagoya, Japan
SOURCE: Yakuri to Chiryo (1973-2000) (1990), 18(7), 2615-29
CODEN: YACHDS; ISSN: 0386-3603
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The suppressive effect of single administrations of TAP-144-SR, a sustained-release formulation, on reproductive function was compared with that of repeated administrations of TAP-144 solution in male Sprague-Dawley rats. In addition, the LH-releasing hormone agonistic activity of the metabolites and analogs of TAP-144 was studied. The results indicate that in contrast to TAP-144 solution repeated administration, TAP-144-SR single administration did not have suppressive effect on reproductive function. Thus, TAP-144-SR will be a useful therapeutic agent for sex hormone-dependent prostate gland cancer.
CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 1, 63
IT 32159-22-1 35925-21-4 57982-77-1, Buserelin **62621-13-0**
65807-02-5, Goserelin 74381-53-6D, TAP-144, metabolites 129244-90-2
129244-91-3 130774-53-7
RL: BIOL (Biological study)
(LH-releasing hormone agonistic activity of TAP-144 vs.)
IT **62621-13-0**
RL: BIOL (Biological study)
(LH-releasing hormone agonistic activity of TAP-144 vs.)
RN 62621-13-0 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 4-D-serine-6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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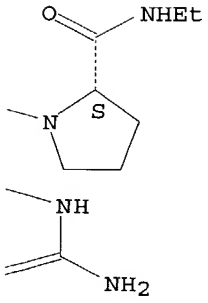


L15 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:82207 CAPLUS
DOCUMENT NUMBER: 108:82207
TITLE: HPLC of leuprolide acetate in injectable solutions
AUTHOR(S): Sutherland, J. W.; Menon, G. N.
CORPORATE SOURCE: Pharm. Prod. Div., Abbott Lab., North Chicago, IL, 60064, USA
SOURCE: Journal of Liquid Chromatography (1987), 10(10), 2281-9
CODEN: JLCHD8; ISSN: 0148-3919
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A stability-indicating HPLC method based on a 5-μ octadecylsilane column and pH 6.5 0.057M aqueous monobasic ammonium phosphate solution-MeCN (77:23 by volume) mobile phase, and UV detection at 220 nm was used for the

determination of leuprolide acetate in injections. Et p-hydroxybenzoate was the internal standard The relative standard deviation was 1.8% and the method was also successfully used for the determination of impurities/precursors occurring during the drug manufacture The drug was more stable at pH 3.3 than at pH 10.3 when heated at 100° for 16 h. Glu1-leuprolide was the major degradation product when the drug was treated with 0.1N HCl at 40° for 48 h.

CC 64-3 (Pharmaceutical Analysis)
Section cross-reference(s): 63

IT 54785-87-4 112642-10-1 **112642-11-2 112642-12-3 112710-56-2 112710-57-3 112710-58-4 112710-59-5**
RL: ANT (Analyte); ANST (Analytical study)
(HPLC of, leuprolide determination in relation to)

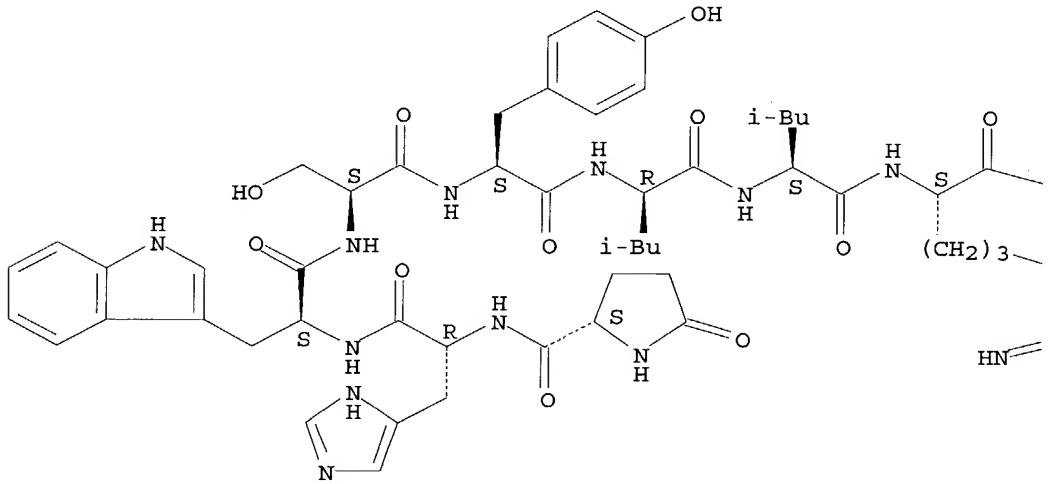
IT **112642-11-2 112642-12-3 112710-56-2 112710-57-3 112710-58-4 112710-59-5**
RL: ANT (Analyte); ANST (Analytical study)
(HPLC of, leuprolide determination in relation to)

RN 112642-11-2 CAPLUS

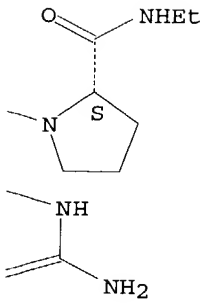
CN Luteinizing hormone-releasing factor (swine), 2-D-histidine-6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



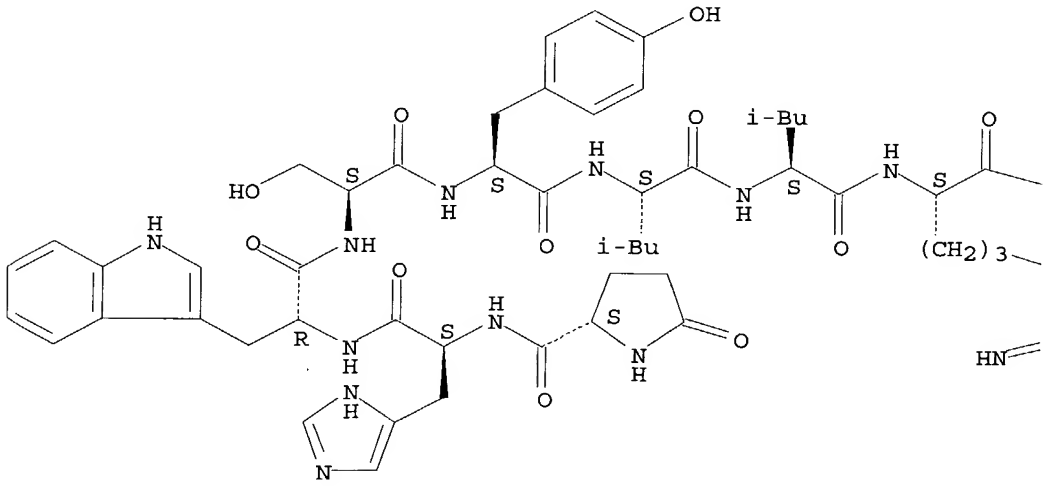
PAGE 1-B



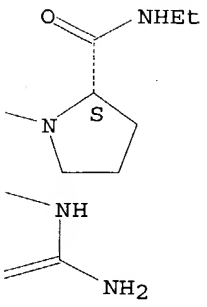
RN 112642-12-3 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 3-D-tryptophan-6-L-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



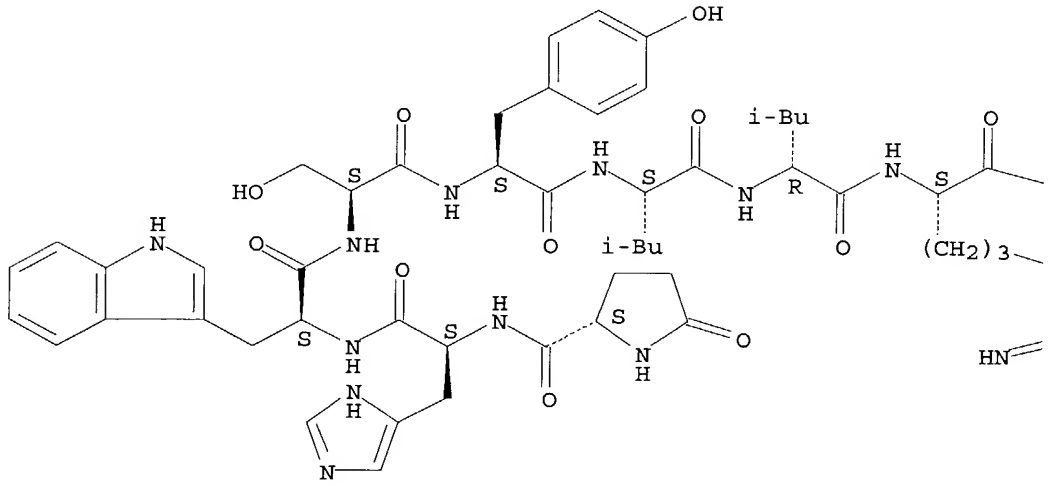
PAGE 1-B



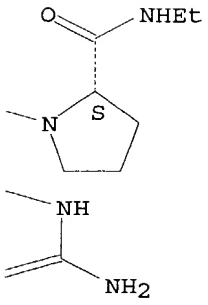
RN 112710-56-2 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 6-L-leucine-7-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



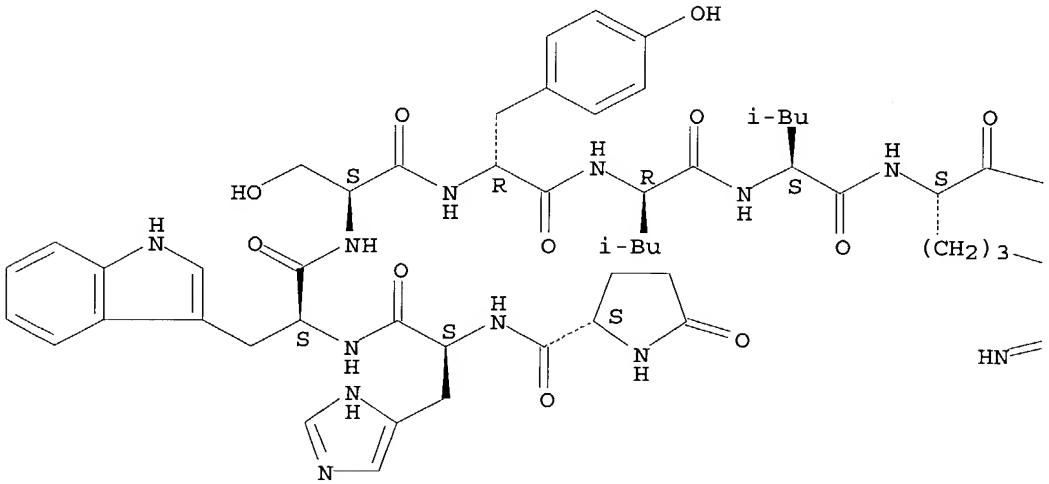
PAGE 1-B



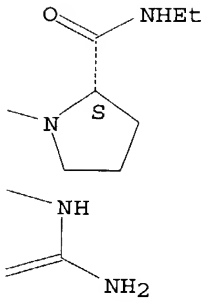
RN 112710-57-3 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 5-D-tyrosine-6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



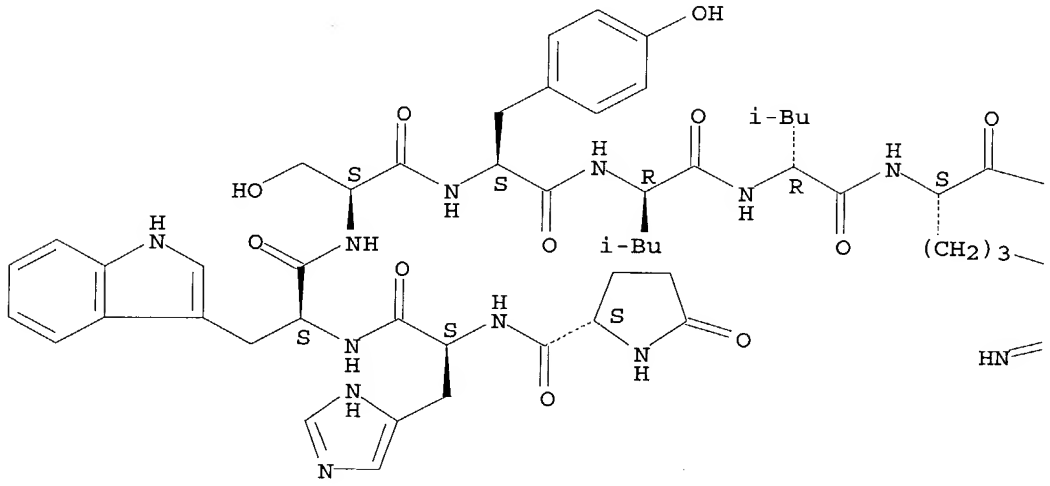
PAGE 1-B



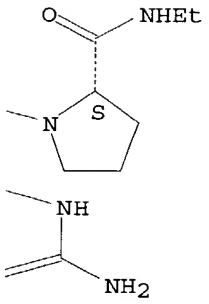
RN 112710-58-4 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 6-D-leucine-7-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



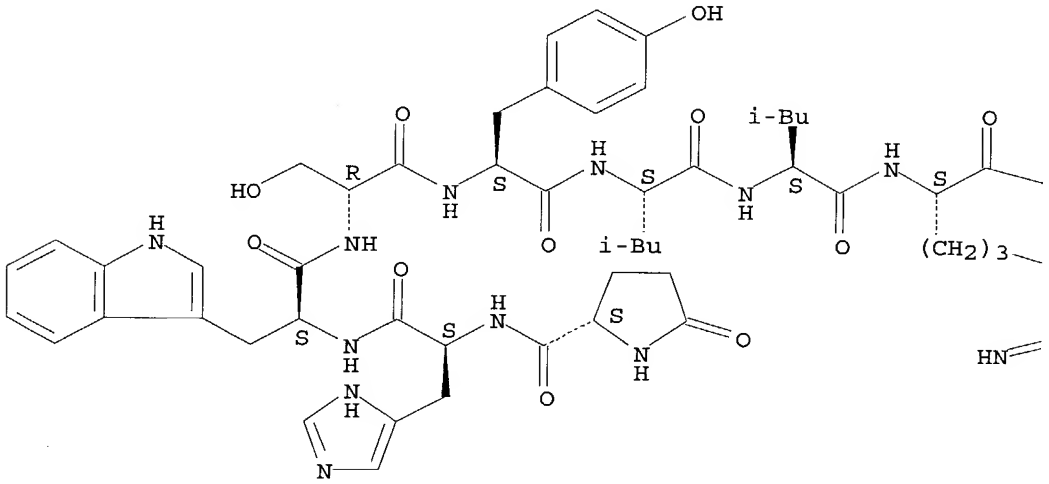
PAGE 1-B

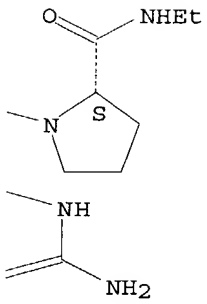


RN 112710-59-5 CAPLUS
CN Luteinizing hormone-releasing factor (swine), 4-D-serine-6-L-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





L15 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1984:73972 CAPLUS
DOCUMENT NUMBER: 100:73972
TITLE: Cyclodextrin formulations of hydrophilic drugs
INVENTOR(S): Hirai, Shinichiro; Okada, Hiroaki; Yashiki, Takatsuka; Uda, Yoshiaki
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd. , Japan
SOURCE: Eur. Pat. Appl., 52 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 94157	A1	19831116	EP 1983-302118	19830414
EP 94157	B1	19870729		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
JP 58189118	A2	19831104	JP 1982-73731	19820430
JP 02019092	B4	19900427		
JP 59021613	A2	19840203	JP 1982-132658	19820728
JP 05024130	B4	19930406		
JP 59148717	A2	19840825	JP 1983-21899	19830211
JP 05024129	B4	19930406		
US 4659696	A	19870421	US 1983-487836	19830422
CA 1218606	A1	19870303	CA 1983-427018	19830429
CA 1218605	A1	19870303	CA 1983-427019	19830429
US 4670419	A	19870602	US 1985-753816	19850708

PRIORITY APPLN. INFO.:
JP 1982-73731 19820430
JP 1982-132658 19820728
JP 1983-21899 19830211
US 1983-487831 19830422

AB Hydrophilic drugs, which are poorly absorbed by the digestive tract, can be absorbed readily from the nasal cavity, vagina, or rectum when given with a cyclodextrin. The drugs include polysaccharides, aminoglycoside and β-lactam antibiotics, peptides, and nucleic acid drugs. About 200 mg porcine insulin [9004-10-8] was dissolved in 8 mL pH 7.4 isotonic phosphate buffer, mixed with 500 mg α-cyclodextrin [10016-20-3] and 20 mg chlorobutanol, and diluted to 10 mL with saline. Administration as a

nasal spray gave a much greater absorption of insulin than from a solution containing no cyclodextrin.

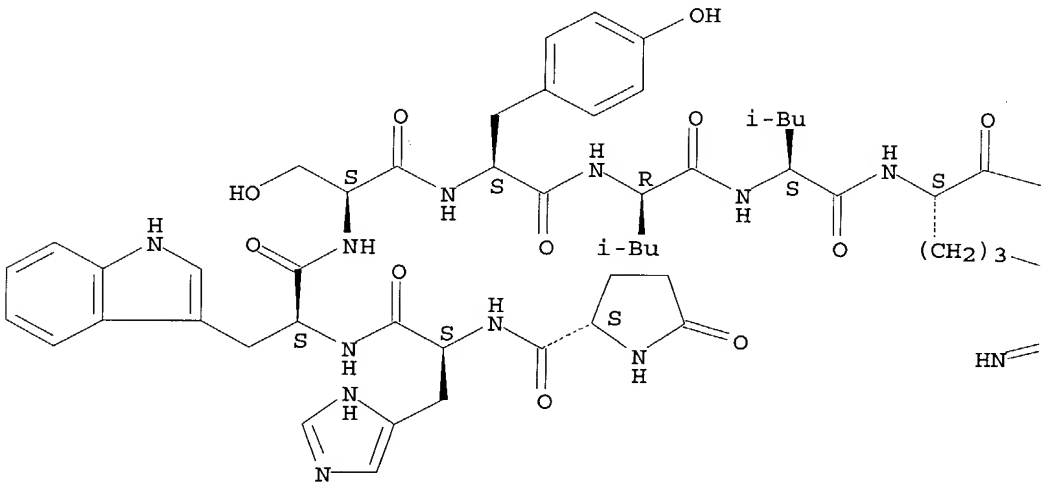
IC A61K009-18; A61K031-715; C08B037-16
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 2
IT 51-21-8 987-78-0 9041-08-1 25389-94-0 27164-46-1 28002-18-8 66309-69-1 77026-81-4 **88793-81-1**
RL: BIOL (Biological study)
(absorption of, by rectum, cyclodextrins increase of)
IT **88793-81-1**
RL: BIOL (Biological study)
(absorption of, by rectum, cyclodextrins increase of)
RN 88793-81-1 CAPLUS
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, acetate (salt) (9CI) (CA INDEX NAME)

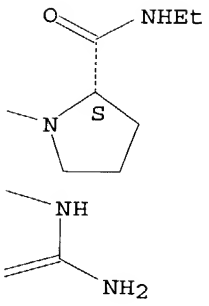
CM 1

CRN 53714-56-0
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

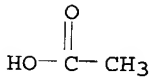
PAGE 1-A





CM 2

CRN 64-19-7
CMF C2 H4 O2



L15 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1977:155987 CAPLUS
DOCUMENT NUMBER: 86:155987
TITLE: Peptides
INVENTOR(S): Schally, Andrew V.; Coy, David H.
PATENT ASSIGNEE(S): USA
SOURCE: Ger. Offen., 42 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2625843	A1	19761223	DE 1976-2625843	19760609
DE 2625843	C2	19850328		
US 4010125	A	19770301	US 1975-586437	19750612
US 4018726	A	19770419	US 1975-586436	19750612
US 4024121	A	19770517	US 1976-652945	19760127
AU 500087	B2	19790510	AU 1976-14524	19760602
CA 1065859	A1	19791106	CA 1976-254039	19760604
BE 842857	A1	19761213	BE 1976-167844	19760611
SE 7606692	A	19761213	SE 1976-6692	19760611
SE 427031	B	19830228		
SE 427031	C	19830609		
FR 2313940	A1	19770107	FR 1976-17854	19760611
FR 2313940	B1	19790420		

JP 52031073	A2	19770309	JP 1976-69247	19760611
JP 60022720	B4	19850603		
GB 1535602	A	19781213	GB 1976-24273	19760611
CH 615662	A	19800215	CH 1976-7474	19760611
SU 668594	D	19790615	SU 1976-2385903	19760729
CA 1067487	A1	19791204	CA 1979-322018	19790221

PRIORITY APPLN. INFO.:

US 1975-586436	19750612
US 1975-586437	19750612
US 1976-652945	19760127
CA 1976-254039	19760604

AB H-pyroGlu-His-Trp-X-Tyr-X1-Leu-Arg-Pro-R (I; R = Gly-NH2, X = Ser, X1 = D-Trp, D-Phe; R = NHEt, X = D-Ser, X1 = D-Leu), LH-releasing hormone/FSH-releasing hormone analogs, were prepared by the solid-phase method. Thus, H-pyroGlu-His(Tos)-Trp-Ser(CH2Ph)-Tyr(CO2CH2C6H4Br-2)-D-Trp-Leu-Arg(Tos)-Pro-Gly-benzhydrylamine resin was prepared and cleaved with HF to give I (R = Gly-NH2, X = Ser, X1 = D-Trp).

IC C07C103-52

CC 34-3 (Synthesis of Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 63

IT 9034-38-2DP, analogs 9034-40-6DP, analogs 57521-78-5P 57773-63-4P
62621-13-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

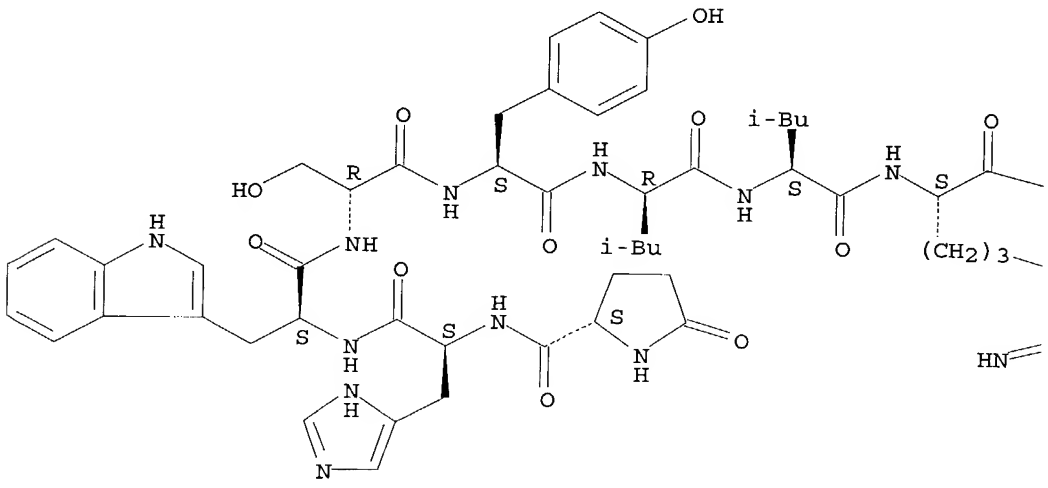
IT **62621-13-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

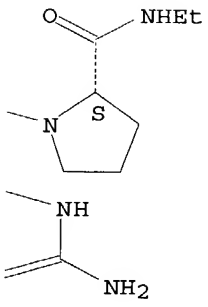
RN 62621-13-0 CAPLUS

CN Luteinizing hormone-releasing factor (swine), 4-D-serine-6-D-leucine-9-(N-ethyl-L-prolinamide)-10-deglycinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A




O
NHEt
N
S
NH
NH2

=>